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1949 CURRENT THERAPY

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CASE: 49*

20-year-old woman suffers severe dysmenorrhea of six years' duration. Analgesics, sedatives and surgery fail to control symptoms. Intramuscular injection of DEPROPANEX *deproteinated pancreatic extract relieves pain; symptoms diminish during subsequent periods.*

L. B., a 20-year-old woman, had suffered severe dysmenorrhea since the onset of the menarche at 14 years of age. She was unmarried and had had no pregnancies. During her menstrual periods, she was consistently incapacitated for from one to three days.

Administration of estrogens and sedatives provided little or no relief. Hospitalization and study of her condition on several occasions failed to disclose any tangible cause for such severe dysmenorrhea.

Operative intervention was finally decided on, and a presacral neurectomy was performed. However, before the patient recovered completely from the operation, her menstrual period occurred. She suffered much pain and no improvement was noted in her condition when compared with the dysmenorrhea experienced prior to the operation.

When pain continued unabated for four hours despite administration of sedatives and analgesics, it was decided to administer DEPROPANEX deproteinated pancreatic extract, a nonnarcotic spasmolytic agent. Two cubic centimeters of DEPROPANEX were injected intramuscularly and partial relief of pain was experienced in fifteen minutes. In one hour the patient was completely free of pain.

Because of its antispasmodic effect on the uterine muscle, DEPROPANEX was administered during three subsequent menstrual periods. Each time the symptoms 'gradually diminished in severity, and the patient was less incapacitated. At her last period, dysmenorrhea symptoms had abated to such an extent that no medication was required.

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*Actual case record

Exophthalmos

THE SCHNEIDER FOUNDATION EYE PRESENTATION

DERRICK VAIL*

NORTHWESTERN UNIVERSITY MEDICAL SCHOOL, CHICAGO

EXOPHTHALMOS or ocular proptosis may be the result of many different causes. Although it is invariably but a sign of some underlying and responsible condition, it often is the most serious sign of that state and as such deserves special consideration. It is also a sort of common denominator wherein many medical specialties meet and the diagnosis of its cause often requires the cooperation of the ophthalmologist, neurologist, neurosurgeon, roentgenologist, otorhinologist, and general physician.

One must decide in every case whether the proptosis is a true or apparent one. This may be difficult. Apparent proptosis may be protrusion of the lids (1) as a result of fat, (2) a familial feature, (3) or facial asymmetry. In the presence of swelling and edema or inflammation proptosis may be simulated. Purely ocular causes, such as iritis or glaucoma, and inflammatory lid conditions such as chalazion, hordeolum, lid or lacrimal gland, or sac abscess, frontal sinusitis, periadenitis, trauma, insect stings, trichinosis, and urticaria may yield an apparent proptosis. There are also very rare cases of voluntary or semi-voluntary forms of ocular proptosis (Figure 1).

In some cases where there is an enophthalmos or retraction of the globe within the orbit, such as is seen in Horner's syndrome or fracture of the floor of the orbit, for example, the opposite eye by comparison may appear to be proptosed. Likewise, when there is a slight ptosis of the upper lid, the other eye may appear to be exophthalmic. Nor is it unusual to see a patient from time to time who shows a retraction of the upper lid without exophthalmos, which may be unilateral and due to a past or present thyrotoxicosis.

The determination of a true proptosis is made by measurement of the degree of exophthalmos either with a device known as the Hertel exophthalmometer or by means of a transparent lucite ruler called the Luedde exophthalmometer. These instruments permit one to make a measurement of sufficient clinical accuracy to record the variations of degree of proptosis from time to time. A difference of 3 mm. between the eyes is of significance.

Inspecting the two eyes in a good light and noticing whether the eye is displaced forward vertically or laterally is of importance, because the direction of the proptosis is often helpful in deciding its etiology. In order to discover slight degrees of proptosis, it is sometimes necessary to elevate both of the lids simultaneously and have the patient gaze directly forward. It is often better to stand behind the patient, who is seated on a low chair or stool, and look down across the plane of the orbits from above. It is also wise to sight along the plane of each orbit from the lateral or profile view.

Ocular motility is then tested and limitation of

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Presented November 10, 1948, before the meeting of the Interstate Postgraduate Medical Association of North America, Cleveland, Ohio.

DERRICK VAIL

movement in any direction of gaze is noted. An analysis of the limitation of ocular motion is of value in the diagnosis of the site of the lesion and frequently of its cause.

Palpation and stethoscopic examination of the orbit often gives useful information. It is almost always necessary to have x-ray photographs made. They should include plates of the skull as a whole, the orbits, sinuses, and the optic foramen of both sides. A nose and throat examination is frequently advisable. Blood studies may be indicated, and other laboratory tests such as a determination of the basal metabolic rate are often advisable in order to arrive at the proper diagnosis.

TRUE PROPTOSIS

I. Monocular.

A. Rapid proptosis with edema of the lids—This is seen in: 1. glaucoma, iridocyclitis, panophthalmitis. These conditions need no discussion (Figure 2).

2. Cellulitis of the orbit. Orbital cellulitis presents the signs of inflammation in varying degrees and amounts (Figure 3). It is a secondary manifestation of infection elsewhere and is a syndrome rather than an entity. It may be acute, chronic, mild, or severe. The acute cases develop rapidly with swelling, edema and redness of the eyelids, chemosis of the conjunctiva, tenderness on pressure, and pain on rotation of the eyeball with headache which is chiefly frontal in character. In certain severe cases the intraocular tissues may be involved, producing hemorrhage and vascular alteration due to compression of the central vessels of the retina or thrombophlebitis with edema and exudation into the retina.

This disease may extend and lead to cavernous sinus thrombosis, meningitis, or brain abscess. The cornea may ulcerate as a result of pressure from the conjunctiva and the eyelid. Nasal accessory sinus disease, particularly in the ethmoid and frontal-ethmoid cells, is the main etiologic factor in producing orbital cellulitis (Figure 4).

3. Tenonitis, serous or purulent. An isolated inflammation of Tenon's fascial capsule is a rare condition and there are some who deny its disease entity. It is characterized by chemosis, proptosis, and swelling of the eyelids. The eyeball can be rotated only slightly without causing severe pain. Consequently the patient will keep his eyes in a more or less fixed position. The condition is probably rheumatic in origin, with rapid onset. The purulent form may lead to orbital cellulitis.

4. Thrombosis of the cavernous sinus. The course of this disease, hitherto invariably fatal can best be described by an illustrative report of a case seen before the days of chemotherapy and the anticoagulant drugs.

CASE REPORT

An 8-year-old girl presenting a small hordeolum of the left upper lid was seen. Within four hours severe edema involving the left upper and lower lids occurred. The eyelids became exquisitely tender; the child appeared flushed, with a fever of 103° F. She was admitted immediately to the hospital, where hot foments and supportive treatment were given. The next day the upper and lower lids were tense, chemotic, and reddened. A tender preauricular left gland was noted. That evening her fever rose to 104° F. An edema of the bulbar conjunctiva was present for the first time. The intraocular examination was negative.

The third day there was limitation of the movement laterally, indicating an involvement of abducens nerve. The following day there was limitation of ocular movements in all respects, which increased until total ophthalmoplegia, interna and externa occurred. The retinal veins became distended, the eyeball proptosed for 4 mm., measured with the Hertel exophthalmometer. On the fourth day the right eye-

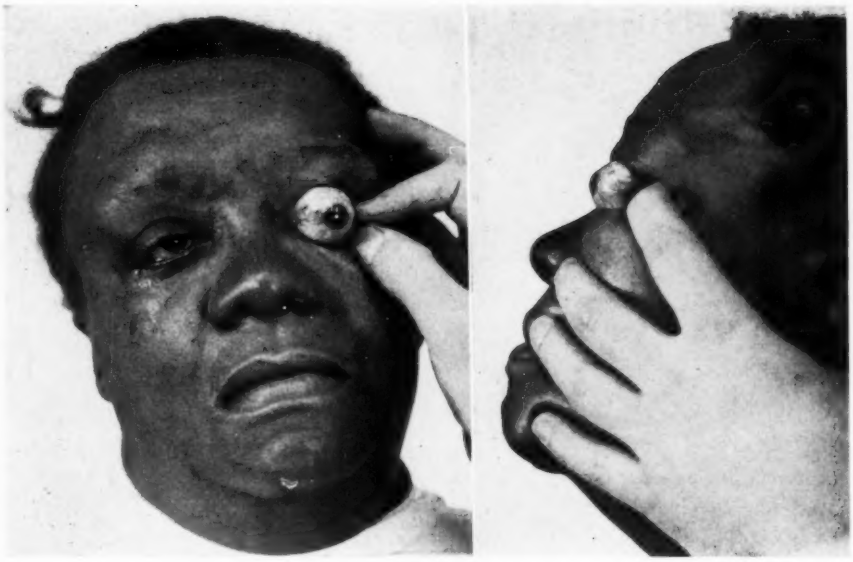

Figure 1. Semi-voluntary ocular proptosis.

Figure 2. Staphyloma of right eyeball. Bilateral blindness. Ophthalmia neonatorum. Apparent proptosis.

Figure 3. Orbital and lid abscess. Subperiosteal.

Figure 4. Pan-sinusitis with orbital involvement. Surgery of sinuses and sutures of lids. Uneventful recovery.

Figure 5. High myopia, bilateral, and familial "full" eyes Apparent proptosis.

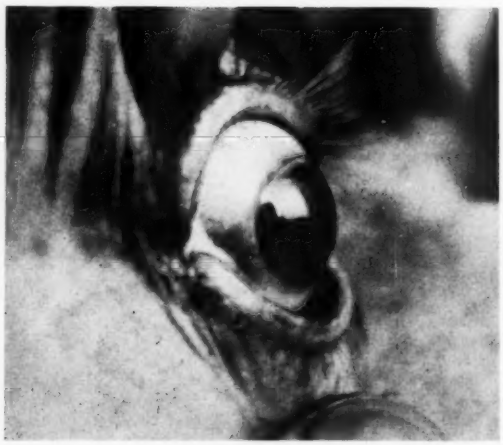

Figure 6. Apparent proptosis due to congenitally enlarged eyeballs. Megalophthalmos anterior.

ball became edematous and somewhat proptosed. The child died on the fifth day.

5. Hemorrhage into the orbit. This is often connected with some systemic disease as in scurvy, anemia, leukemia of the myelogenous type, rickets, and hemophilia. In infants the possibility of scurvy as an etiologic factor must always be considered. Here subperiosteal hemorrhages may occur anywhere in the body, characteristically along the inner aspects of the femur. Occasionally they occur along the orbital bone, and unless the underlying cause is recognized, they may be mistaken for orbital neoplasms.

Exophthalmos in rickets is perhaps more often due to periosteal proliferation, although it may be caused by hydrocephalus or subperiosteal hemorrhages. In severe compression of the thorax, hemorrhage may appear not only in the orbit but under the skin of the face and neck, under the conjunctiva and in the retina, even in the absence

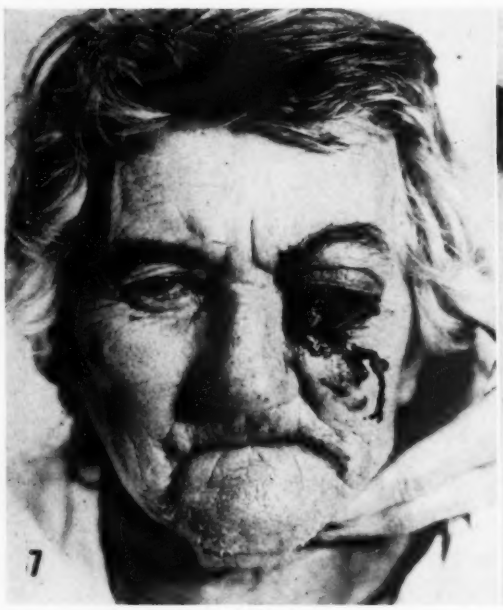

Figure 7. Melanotic sarcoma (melanoma) left eye with rupture of the cornea and orbital extension.

Figure 8. Side view of patient in Figure 7.

Figure 9. Aneurysm of circle of Willis. Proptosis and third nerve paralysis. Woman aged 62.

Figure 10. Proptosis, left eye. Result of tenotomy of internal rectus muscle many years ago.

Figure 11. Unilateral thyrotoxic exophthalmos. Burnt out thyroid. Girl aged 16.

Figure 12. Pulsating exophthalmos left. Traumatic. Cavernous sinus arteriovenous aneurysm.

of any injury to the head. Orbital hemorrhages may occur during paroxysms of coughing and in asphyxiated newborn infants.

B. Gradual proptosis without edema—1. Congenital malformation of the orbit. A defect in the roof of the orbit allows the brain and meninges in the anterior fossa to herniate into the orbit producing an exophthalmos which sometimes pulsates. It is called a posterior orbital encephalocele or meningocele. The more common anterior encephalocele or meningocele gives rise to a lateral displacement of the globe and less frequently to exophthalmos. These congenital defects of the orbital wall may not be evident until a considerable time after birth, sometimes as late as ten years.

2. Ocular enlargement. High myopia (Figure

Figure 13. Circoid aneurysm involving both orbits.

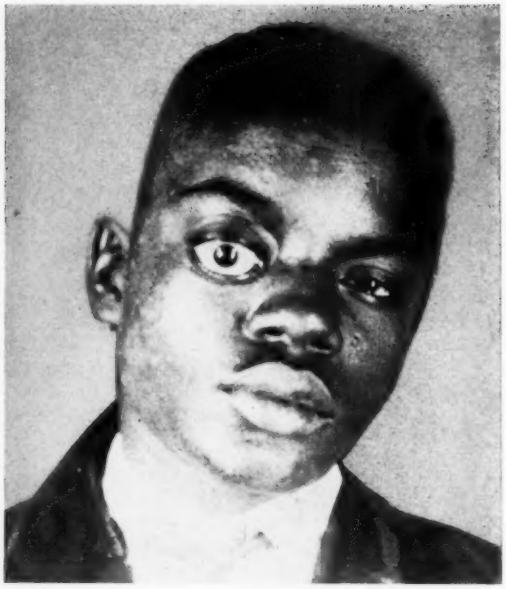

Figure 14. Primary tumor of right optic nerve. Glioma. Note the proptosis is directly forward.

5), buphthalmos, anterior megalophthalmos (Figure 6), sarcoma of the choroid perforating posteriorly or anteriorly (Figures 7 and 8.)

3. Paralysis of the third nerve with loss of muscle tone (Figure 9). A complete tenotomy of one of the rectus muscles, for example, in a squint operation may produce a mild proptosis of 2 to 3 mm. (Figure 10).

C. Unilateral proptosis with central displacement—1. Thyrotoxic (Figure 11), thyrotrophic exophthalmos.

2. Vascular causes: arteriovenous aneurysms or pulsating exophthalmos (Figure 12). This may be either spontaneous or arise, as is most frequently the case, from trauma. It is not difficult of recognition and the treatment is surgical with ligation of the common carotid or some means of compression of the carotid arteries. Varicose orbital veins, circoid aneurysm of the orbit (Figure 13), nevi, or angiomata are other vascular lesions causing proptosis.

3. Tumors of the optic nerve. The motility of the eyeball is less impaired than one would expect from exophthalmos due to other causes. Visual acuity diminishes very soon as a rule. The pressure on the optic nerve may cause atrophy or even papilledema. The tumor may be primary or secondary. It may be gliomatous (Figure 14) or from fibrous tissue. In the intravaginal space endotheliomas may be found. Usually tumors arise in the orbital part of the nerve, but they may also develop in the intracranial portion, generally in the chiasm. They grow slowly and are almost never malignant. (Meningioma, arising from the optic foramen) (Figures 15, 16, 17, and 18).

4. Cysts in the orbit: congenital—(a) cysts developed as the result of herniation of the brain or the meninges; (b) serous cysts, usually associated with microphthalmos or the encystment of a congenital coloboma of the choroid; (c) dermoid cysts. These may extend along the floor or roof of the orbit and push the eye forward. They are generally not difficult of recognition.

Acquired—(a) cysts which are developed as the result of exudation and the inclusion of epithelial tissue as a result of trauma or around neoplasms; (b) parasitic cysts (hydatid or Cysticercus).

5. Neoplasms in the orbit: (a) benign, as a

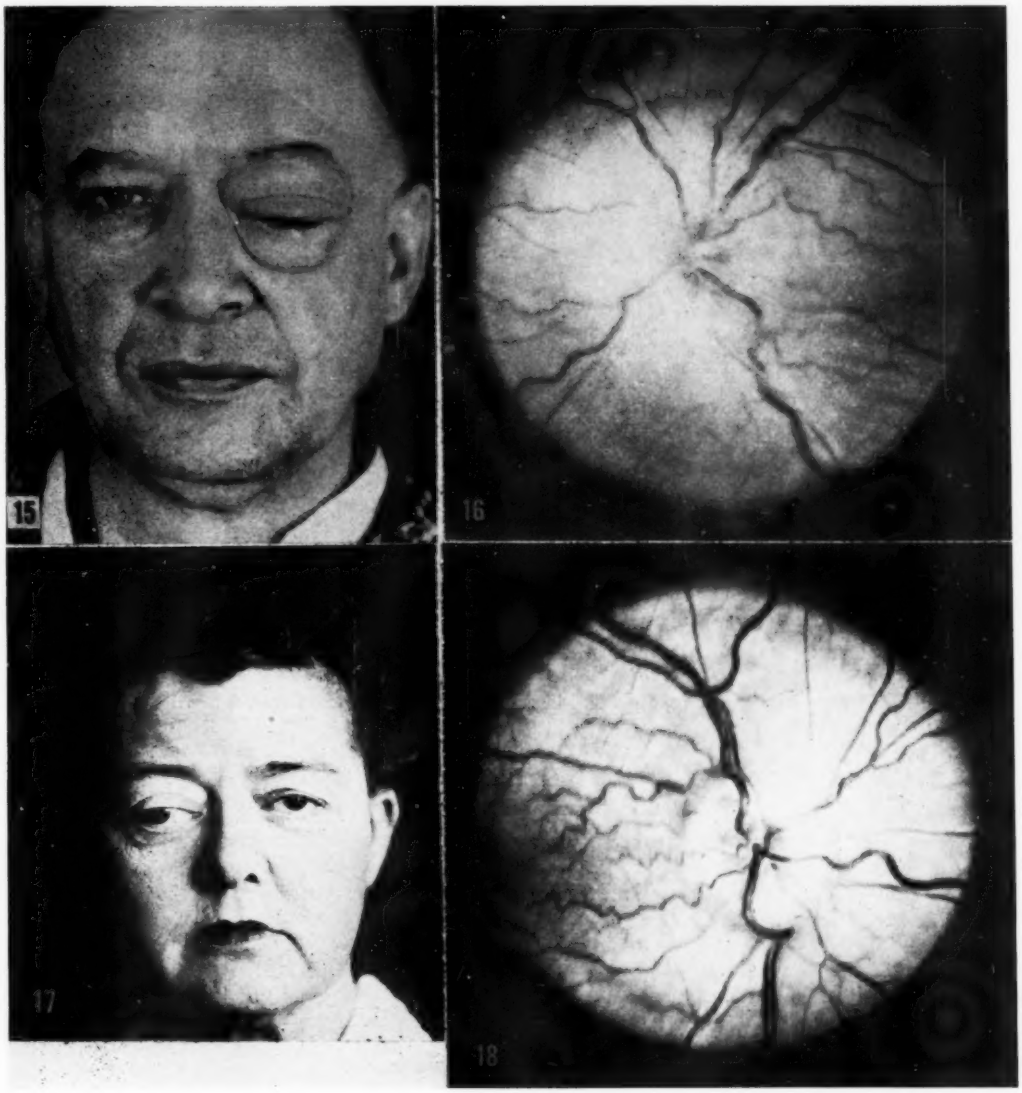

Figure 15. Meningioma arising intracranially and extending into orbit through the optic foramen.

Figure 16. Choked disk. Patient in Figure 15.

Figure 17. Meningioma, intracranial, extending into orbit along optic nerve.

Figure 18. Optic nerve. Patient in Figure 17. Note elevation of nerve head, result of tumor involvement of nerve sheaths up to the papilla.

Figure 19. Mixed tumor lacrimal gland. Woman aged 48.

Figure 20. Mixed tumor lacrimal gland. Man aged 46. Death two years later, pelvic metastases.

plexiform neuroma; (b) malignant, mixed tumor of the lacrimal gland (Figures 19 and 20), primary sarcomas (Figure 21), metastatic neoplasms (Figure 22), chloroma; (c) pseudotumor. These are mysterious affairs and are not too uncommon. They are usually seen in persons past middle age and are of low grade inflammatory origin. A pseudotumor tends to regress spontaneously.

6. Foreign bodies.

D. Unilateral proptosis with lateral displacement—1. Mucocele from the sinus. Rollet, in 1896, first suggested this term. It is met with especially in subjects from 25 to 40 years of age and begins slowly and insidiously. It is a result of repeated attacks of more or less attenuated infections of the mucosa. When the mucocele arises from the frontal sinus, which is most frequently the case, the eye as a rule is deviated down and outward (Figures 23 and 24). The swelling can easily be palpated and there is a curious deformity of the roof of the nose first described by Rollet. The bridge of the nose, instead of being concave from above downward and convex transversely presents a flat surface whose width is increased by about 5 cm. The upper lid is smoothed out and the palpebral fissure is narrowed. Rollet considers this pathognomonic of a distention of the frontal sinus by mucus, pus, or benign neoplasm; that is to say, where there is a very slowly developing process at work.

Corneal complications can follow if there is exposure. When the mucocele springs from the posterior ethmoidal cells it produces a protrusion directly forward similar to that caused by tumors in the depth of the orbit although not so marked. The deviation, however, is usually down and out.

2. Neoplasms from the sinuses (Figure 25).

3. Bony exostosis from the wall of the orbit. This is encountered in osteoma and following certain meningiomas.

4. As a result of nasal surgery. This is particularly apparent in radical frontal operations where the pulley or trochlea has been disturbed.

Figure 21. Gradual, painless swelling of right upper lid with moderate proptosis. Diagnosis lymphosarcoma of lacrimal gland.

Figure 22. Tumor right orbit. Metastatic C. A.

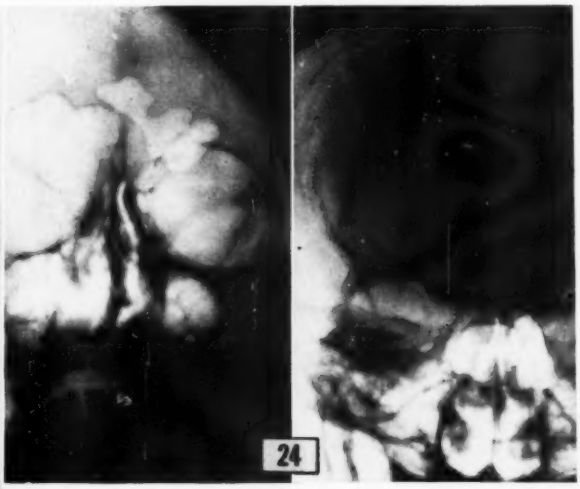

Figure 23. Mucocele of right frontal sinus, with extension into orbit. Note deviation of eye down and outward.

Figure 24. X-ray photograph of patient in Figure 23. Mucocele of right frontal sinus.

Figure 25. Sarcoma right maxillary sinus, orbital invasion.

5. Orbital osteoperiostitis. This is most frequently the result of sinus disease.

6. Meningocele.

7. Emphysema of the orbit.

II. Binocular exophthalmos.

1. Congenital or as a familial trait.

2. Tower skull, as the result of too early closure of fontanelles, which in addition to the marked proptosis found often leads to optic atrophy as the result of pressure (Figures 26 and 27).

3. Graves' disease or exophthalmic goiter (Figures 28 and 29). Particular attention is directed to the malignant or thyrotrophic type of exophthalmos which at times is seen to follow the removal of the thyroid gland. Here a moderate proptosis may suddenly become a most severe one. It is considered due to the fact that the pituitary gland, released of its inhibitory action by the thyroid goes wild. A number of these patients show acromegalic fascies (Figure 31). Myasthenia gravis may be present simultaneously. The prostigmine test should be given to every patient with thyrotrophic exophthalmos.

4. Neoplasms arising in the ethmoid or sphenoid sinuses extending to both orbits. Rare cases of bilateral orbital neoplasms (Figure 30).

5. Double sided sinusitis. The sinuses play a most important part in the production of proptosis. It might be well, therefore, to digress for a moment and discuss the more or less constant signs pointing to sinus disease. These are: (a) lacrimation, associated with proptosis, which can be explained, either as a result of pressure on the lacrimal gland, or a functional disturbance of Horner's muscle, the tensor tarsi; (b) proptosis in a sinus disease is a very important sign and is fairly constant.

When an eye projects downward, outward, and forward, suppuration of the frontal sinus or ethmoid is likely. A deviation downward and inward suggests frontal sinus or lacrimal gland suppuration. Proptosis with deflection upward is not usually due to a suppurating sinus, for an infected antrum rarely does this. Here one should always suspect malignant disease, which is usually accompanied by suppuration. One should also bear in mind that malignant disease arising in the sinuses can invade the orbit and cause symptoms similar to those described.

6. Neurofibroma (von Recklinghausen).

7. Myasthenia gravis. The prostigmine test will reveal the true nature of the proptosis in this event. It may be associated with the thyrotrophic type of exophthalmos.

8. Cavernous sinus thrombosis.

9. Mikulicz' disease.

10. Sarcoidosis.

11. Cranio-orbito-facial malformations: (a) hereditary dysostosis or Crouzon's disease; (b) multiple xanthomatosis or Schuller-Christian disease. This is a generalized disease in which tumorous masses of reticular cells are engorged with lipids, predominantly cholesterol. Occasionally the condition is associated with diabetes insipidus and defects of the membranous bone; (c) other rare forms.

COMMENT AND CONCLUSIONS

In a diagnosis of proptosis and its etiology we must first consider whether or not there is a true exophthalmos. This can best be determined by looking down from above along the plane of the forehead. Secondly, how much proptosis is there? Measurements that are clinically accurate can be

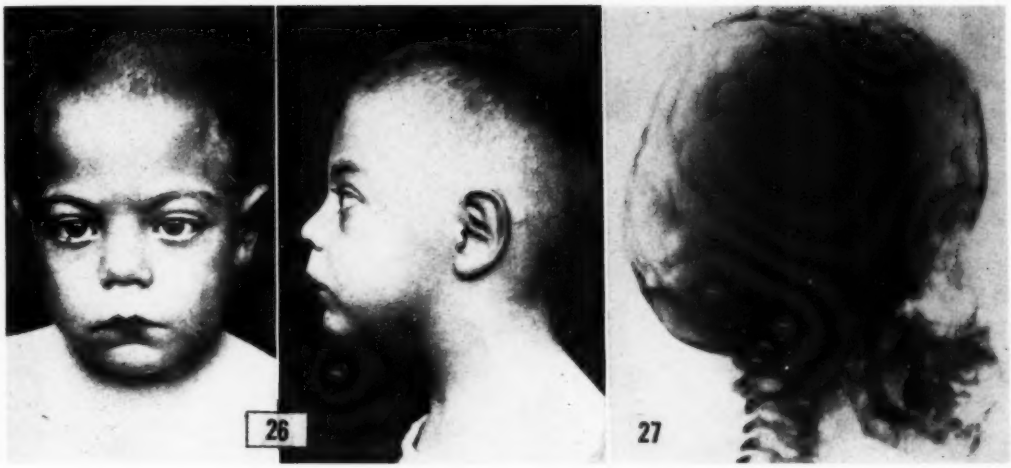

Figure 26. Tower skull.

Figure 27. X-ray photograph of patient with tower skull.

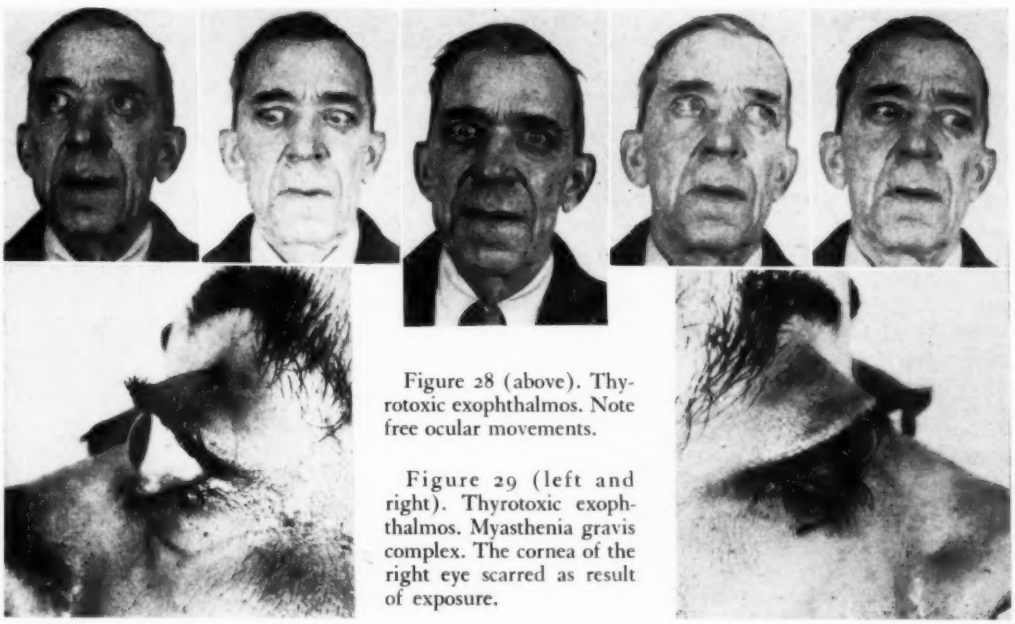

Figure 28 (above). Thyrotoxic exophthalmos. Note free ocular movements.

Figure 29 (left and right). Thyrotoxic exophthalmos. Myasthenia gravis complex. The cornea of the right eye scarred as result of exposure.

Figure 30. Bilateral neurocytic glioma orbit. Totally blind. No cranial involvement.

Figure 31. Thyrotrophic exophthalmos. Note the pituitary fascies. Marked edema of the lids and conjunctiva.

made easily with the Hertel or Luedde exophthalmometers. Third, in what direction is the proptosis? The direction of the deviation of the eyeball is a valuable and reliable guide to the situation of the lesion. If the eyeball is pushed straight forward without deviation look for the lesion within the ocular muscle cone at the orbital apex; down and out, investigate the frontal sinus; upward, suspect the maxillary sinus; and downward and somewhat inward, the ethmoids.

Fourth, is there a tumor present; can it be palpated, and does it reveal a bruit when the stethoscope is applied? Fifth, every case of unilateral proptosis and most cases of bilateral proptosis should have an x-ray photograph of the skull. A solid tumor may be present; the optic foramen may be enlarged. There may be a dehiscence or absence of part of the orbital bony margins or walls, particularly of the roof of the orbit.

Sixth, and perhaps most important, a careful history should be taken in all cases, with particular emphasis on the duration and rapidity of onset of exophthalmos. Seventh, consultations with colleagues in the appropriate specialty fields are necessary in most cases. This particularly applies to the otolaryngologist whose assistance at operation may be most helpful.

Isoimmunization by the Rh Factor

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THE Rh factor, unlike other human blood properties M, N, or P, is important clinically only because of its capacity to induce isoimmunization either by transfusion, intramuscular injection, or by the transfer of fetal blood across the placenta. In other words, the Rh factor is "antigenic" for individuals whose red blood cells lack this factor. The latter, known as Rh negative, respond by the production of antibodies known as anti-Rh. This subject has become prominent because this antibody, when produced by an Rh negative mother, has been shown to be responsible for the symptoms of blood destruction in the condition known as hemolytic disease of the fetus and newborn (erythroblastosis fetalis).

The Rh factor splits each of the four blood groups into two unequal subtypes, Rh positive (85 per cent) and Rh negative (15 per cent), so that for transfusion purposes it now becomes important to think in terms of eight blood types. So far as the obstetrician or general practitioner is concerned, their obstetric patients and those requiring transfusion will be protected if routine Rh tests are carried out in these cases.

In the event of transfusion requirements, all patients found to be Rh negative must receive group compatible Rh negative blood. Unless these precautions are taken, the 15 per cent Rh negative patients may be immunized as indicated by the appearance of anti-Rh antibodies. If such patients require additional transfusions, they will be subject to severe or perhaps fatal transfusion reactions unless Rh negative blood is selected. Rh negative female patients, particularly young girls, if already immunized by previous administration of blood either intramuscularly or intravenously, may lose all their infants many years later from hemolytic disease of the fetus and newborn. Immunized Rh negative mothers requiring blood transfusions may develop severe reactions and complete anuria if transfused the first time with Rh positive blood.

The Rh factor is one of several blood properties which contribute toward the concept of individuality of human blood. Aside from the factors A and B which make up the four blood groups, there are the agglutinable properties M, N, and P, the subgroups of groups A and AB, the three sets of Rh-Hr factors, and still other properties. It is significant that each one of these factors is a normal property of human blood, the incidence of which may vary in different racial groups. The individuality results from the permutation and combination of these several serologic properties. It is known that at least some of these agglutinogens may also be present in tissue cells so that one may assume the existence of a similar individuality in the tissue cells. From a theoretical standpoint, these considerations offer an explanation for the failure of tissue transplants and for the success of autotransplants.

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Presented November 11, 1948, before the meeting of the Interstate Postgraduate Medical Association of North America, Cleveland, Ohio.

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It is now definitely established that in about 93 per cent of all cases of hemolytic disease, the mother's blood fails to agglutinate with standard anti-Rh sera, and that their sera contains the corresponding antibody which exerts its harmful effect not only in utero but also in the neonatal period. In the remaining 7 per cent, the mother is Rh positive, but she is lacking another blood factor which is present in the father's blood and genetically transmitted to the offspring. The factors involved in this smaller group are quite numerous, and it is not surprising that this aspect of the subject has proved so confusing to the physician.

There are at least two additional variants of the Rh factor, the three corresponding Hr factors, the factors A or B (nonsecretor form) and rarely still other agglutinable properties which like the Rh factor have the capacity to act as foreign material to certain selected mothers. In all instances, the mother reacts to the antigenic properties in the fetal blood by producing the corresponding antibody which finds its way into the fetal circulation and may persist in the infant's tissue spaces during the neonatal period. The end result is destruction of fetal or infant's blood which is the characteristic clinical and pathologic feature of hemolytic disease of the newborn.

The concept that fetal red blood cells may pass into the maternal circulation was first mentioned by Levine and Stetson in 1939 in explanation for the occurrence of a severe intragroup transfusion reaction at the very first transfusion of a woman who had a previous stillbirth and whose current pregnancy terminated in intra-uterine fetal death. Presumably, the atypical antibody, later identified as anti-Rh, must have been present prior to the transfusion. The new blood factor fully described with the aid of this mother's agglutinin could not be identified by any name, but it was later shown to be identical with the factor common to rhesus and human blood described and named "Rh" by Landsteiner and Wiener in 1940.

THE mechanism of transplacental transfer of fetal red blood cells during the course of pregnancy will be discussed below. At this point, it may suffice to state that minute quantities of fetal blood are believed to pass into the maternal sinuses in every normal pregnancy.

In this section the serologic aspects will be presented in terms of two variations, Rh positive (Rh+) which reacts with anti-Rh_0 or anti-D and Rh negative (Rh−) which lacks the Rh_0 or D factor, but contains another property known as Hr_0 or d. (The corresponding antibody produced by an Rh+ mother is known as anti-Hr_0 or anti-d.) The distribution of this important diagnostic serum, anti-Rh_0 (anti-D) for the screening of Rh+ and Rh− individuals is now controlled by standards laid down by the N.I.H. It must be potent (at least 32 activity units) and give clearcut differentiation of bloods possessing (Rh+) and bloods lacking the factor (Rh−).

Taking into account the Rh factor and the four blood groups, eight types must now be the basis for selection of donors for transfusion purposes. These are presented in Table 1.

The specific antibodies, anti-A and anti-B, which define the four blood groups, are normal properties of human serum in contrast to anti-Rh antibodies which may be produced by some, but not all, Rh− individuals who receive Rh+ blood via any one of several routes. While an Rh− male may receive the first one or two transfusions of Rh+ blood with impunity, subsequent transfusions may result in severe or fatal reactions. It is, of course, essen-

TABLE 1

THE CLINICALLY IMPORTANT EIGHT BLOOD TYPES

Serum A (anti-B)	0		0		+		+	
Serum B (anti-A)	0		+		0		+	
Group	0		A		B		AB	
Incidence in White Race	45		41		10		4	
	38	7	35	6	8.5	1.5	3.4	0.6
Reactions with anti-D: Rh	+	−	+	−	+	−	+	−

tial to prevent the production of antibodies (isoimmunization) in all Rh− individuals requiring transfusions by the simple expedient of using Rh− donors.

The role of the Rh factor in the pathogenesis of hemolytic disease of the fetus and newborn was established in a statistical study which revealed a very striking deviation in the distribution of the Rh factor in mothers of affected infants from that of a normal (white) population (Table 2).

TABLE 2*

STATISTICAL PROOF

	Rh+	Rh−
Random population, male or female	85	15
350 mothers of erythroblastotic infants	7	93
204 husbands of Rh− mothers	100	0
139 affected infants of Rh− mothers	100	0

*After Levine.

The incidence of hemolytic disease of the newborn in various races differs and is in direct proportion to the incidence of Rh− individuals in any given population (Table 3).

TABLE 3

RACIAL INCIDENCE OF HEMOLYTIC DISEASE

	Per Cent		Incidence of Incompatible Matings	Incidence of Hemolytic Disease
	+	−		
White	85.0	15.0	12.8	2.1
Negro	95.5	4.5	4.3	0.7
American Indians	99.2	0.8	0.8	?
Chinese	99.3	0.7	0.7	Very rare

An incompatible mating is defined as one in which the husband is Rh+ and his wife is Rh−. In the white population, this value is 85 per cent x 15 per cent or 12.8 per cent. Obviously, the end results of isoimmunization by the Rh factor (transfusion reactions and hemolytic disease) are far more important in the white population than in Chinese or American Indians.

TABLE 4

HEMOLYTIC DISEASE IN THE FIRST RH+ INFANT IN RH− WOMEN

	Transfusion History	
	Positive	Negative
Number of cases	19	9
Severity of disease		
mild	1	5
severe	6	4
fetal death	12	0

Hemolytic disease in the firstborn is said to occur very rarely. As a rule, one or more pregnancies with an Rh+ fetus are required before the Rh− mother will produce antibodies. A notable exception to this rule is the group of women who at any time prior to their pregnancies received a transfusion or intramuscular injection of Rh+ blood (Table 4).

THERE is reason to believe that women who do not give a history of transfusion may have received many years previously one or more intramuscular injections of blood. This therapeutic measure was frequently used in the days before vitamin K and human globulin were made available for the prevention or therapy of hemorrhagic and contagious diseases. More recently, histories of such injections—as little as 10 cc.—could be elicited in several instances in which the firstborn was affected.

Rh− girls transfused indiscriminately as they have been in the past are thus deprived of the several factors of safety which tend to diminish the incidence of the disease. With intervals of nine to fourteen years between the "antigenic stimulus" of a transfusion or intramuscular injection and the first pregnancy, one may well assume that the damage to the fetus is not caused by residual antibodies which are evanescent in character but rather by renewed immunization. On renewed contact with the antigen in fetal blood during the course of the first pregnancy, even many years later, the antibody-producing cells of the reticuloendothelial system respond far more rapidly. This series of events serves to illustrate the "recall" phenomenon which is known in the serologic literature as the "anamnestic" reaction.

Taking into account Rh tests as well as clinical and pathologic findings, hemolytic disease occurs once in 1:200 full-term pregnancies. Since 93 per cent of cases occur in the incompatible mating of

an Rh+ father with an Rh- mother, the incidence in these incompatible matings (85 x 15)—13 per cent of all matings—is 200/7.7 or 1:26 full-term pregnancies.

Thus, there are several factors of safety which tend to diminish the incidence of hemolytic disease: (1) the current tendency to small families; (2) the failure of many Rh- women to produce antibodies readily; and (3) a high incidence of heterozygous husbands.

Most Rh- women will require at least three or more pregnancies with Rh+ fetuses before a sufficient degree of isoimmunization is attained. In other words, the vast majority of Rh- mothers are resistant to the production of antibodies and it is assumed that, as in the experimental animal, the capacity to produce antibodies is dependent upon certain genetic properties. There are numerous instances of Rh- mothers who delivered six or more normal Rh+ infants and others who were previously transfused, but all their Rh+ infants were free from hemolytic symptoms.

In more than half of the incompatible matings, the husband is heterozygous so that 50 per cent of their offspring will be Rh- and these pregnancies cannot provide the required antigenic stimulus. In these matings, a greater number of pregnancies are required to induce a sufficient degree of isoimmunization.

In short, the vast majority of affected infants are supplied by only a small number of Rh- mothers. Were every Rh- mother of an Rh+ infant immunized, the incidence of hemolytic disease would be considerably higher than 1:26 full-term pregnancies. Furthermore, not every Rh+ infant of an immunized Rh- mother need be affected. In these instances, it is assumed that antibodies appeared late in the course of the pregnancy and there was not a sufficiently long interval of intrauterine passage of maternal antibodies. One may anticipate, however, an unusually severe form of hemolytic disease in the following pregnancy.

Hemolytic disease of the fetus and newborn assumes an importance altogether out of proportion to its low incidence because it is the first example in any species of a new cause of fetal and neonatal morbidity attributable to a genetic difference involving a particular antigenic blood property which has a normal incidence in any racial group. The essential feature of this form of fetal and neonatal morbidity is its selective effect on Rh+ infants. Thus, in case of twins, only one of whom is affected, the normal member is invariably Rh-.

Undoubtedly, the same mechanism of transplacental isoimmunization and selective fetal and neonatal morbidity will be found to be operative in many species of animals and the first successful demonstration was already reported in horses. In contrast to the human species, the disease in the foal does not occur in utero because in the herbivorous the young acquire their antibodies not via transplacental transfer but by the ingestion of colostrum.

ANTI-RH ANTIBODIES

The theory of transplacental isoimmunization requires that the serum of all mothers of affected infants contain antibodies specific for the corresponding factor in fetal blood. In the early studies, only about 40 per cent of Rh- mothers had anti-Rh agglutinins in their sera. The failure to demonstrate antibodies in the remaining 60 per cent was attributable to the fact that the test Rh+ blood was suspended in saline. From the combined work of Race, Wiener, and Diamond, it is now established that the anti-Rh antibody occurs more frequently in another form which agglutinates Rh+ cells provided that they are suspended in certain protein media, such as normal human serum or, preferably, bovine albumin.

Considerable confusion has resulted from the arbitrary use of a great variety of terms for the two sorts of antibodies. These are listed below:

Saline agglutinins	Albumin agglutinins
Agglutinins	Agglutinoids (Glutinins)
Heat-labile antibodies	Heat-stable antibodies
Complete antibodies	Incomplete antibodies
Bivalent antibodies	Univalent antibodies
Early antibodies	Late antibodies
	Cryptagglutinoids
	Conglutinins
	Blocking antibodies
	Coating antibodies

In this discussion, the terms "saline agglutinin" and "albumin agglutinin" will be employed.

In any event, methods are now available for the detection of antibodies produced by Rh- or Rh+ mothers (or donors who submit to a series of injections on a voluntary basis). Once an antibody is detected, additional tests are required to determine its potency and specificity in tests with blood of known antigenic structure. All attempts should

TABLE 5

DETECTION OF ISOIMMUNIZATION
Test Blood — A Mixture of Rh_1 and Rh_2

	Suspended in			
	I	II		
Serum	Saline	Coombs Test on I	Albumin (20%)	
1	0	+++	+++	Albumin agglutinins
2	0	+±	+	Weak albumin agglutinins
3	0	++++	0 (prozone)	Probably another antibody in addition to albumin agglutinins
4	++++	not tested	++++	Saline agglutinins
5	0	0	0	Not immunized

be made to collect large quantities of sera containing potent antibodies of the several varieties.

Tests for detection of antibodies should be carried out in all prenatal cases and for all candidates for transfusions, Rh+ or Rh−. The test blood should be so selected that all 6 Rh-Hr antigens are present, such as is found in a mixture of two group 0 bloods, types Rh_1 and Rh_2.

FROM a practical standpoint, two methods may be employed in routine tests—the slide test or the test tube. The former is suitable for small scale work or in urgent cases while the test tube method is preferable when simultaneous tests of numerous sera must be made.

For the slide test, about a 40 to 50 per cent suspension of the test blood such as is present in (dry) oxalated blood should be employed. One drop of the patient's serum is mixed with one or two small drops of the test blood on a slide which is placed on a warm illuminated surface and rocked slowly from side to side. Readings should be completed after an interval of two minutes.

For the test tube method, it is desirable to test all sera with both saline and albumin suspended cells. A more dilute suspension (2 to 5 per cent) may be used. Readings may be made at the end of one to two hours' incubation at 37°C. The presence of saline agglutinins is indicated by reactions in both tubes while the albumin agglutinin or the so-called blocking antibody will react with the albumin suspended cells only (Table 5).

COOMBS REACTION

More recently, a new technical procedure described by Coombs has proved to be a very valuable adjunct to Rh testing. In the mixture of albumin agglutinins and saline suspended test cells, a visible reaction is not demonstrable but the specific union of the antigen (Rh+ blood) and its antibody has occurred. The antibody present in the globulin fraction of the human serum (mother's or patient's) is chemically united with the Rh antigen on the surface of the red cells and this combination is resistant to repeated washings in saline which is essential for the removal of any excess or uncombined globulin or other serum components. On the addition of a processed anti-human serum (prepared in rabbits or other animals by injection of human serum) to the thoroughly washed red cells, clumping results from the reaction of the globulin-containing antibody on the red cells (antigen) and the anti-human globulin present in the rabbit anti-human serum.

The results with the Coombs test will serve to confirm the findings with the direct reaction with albumin suspended cells. At the same time, it will aid in the detection of so-called prozones due to the presence in the same serum of both agglutinins and blocking antibodies or several varieties of albumin agglutinins (Table 5).

The Coombs reaction is of the greatest value in testing the cord blood in order to determine if the infant's red cells have been specifically saturated or "coated" with maternal antibodies. For reasons still unknown, only albumin agglutinins but not saline agglutinins can be demonstrated on the surface of the infant's red cells. Strongly coated red cells, as indicated by a powerful reaction with the Coombs reagent, will fail to react with anti-D saline agglutinins or only weakly with albumin agglutinins and have been erroneously diagnosed as Rh−. Actually, such blood is Rh+ and it fails to react because all Rh receptors have been saturated for long periods in utero with maternal antibodies.

The Coombs reaction is also useful in the diag-

TABLE 6

THE THREE RH-HR SERA

Incidence of Reactions (Per Cent), Incompatible Matings (Per Cent), and Antibodies Produced

	+	−	Incompatible Matings	Incidence of Antibodies Produced	
Anti-D (anti-Rh_0)	85	15	13	Frequent	93 Per Cent
Anti-d (anti-Hr_0)	63	37	23	Very rare	
Anti-C (anti-rh′)	73	27	20	Very rare*	About 7 Per Cent
Anti-c (anti-hr′)	80	20	16	Occasional	
Anti-E (anti-rh″)	30	70	21	Occasional	
Anti-e (anti-hr″)	97	3	3	Very rare	

*Anti-C occurs more frequently along with anti-D, in which case it is produced by an Rh− individual.

nosis of acquired hemolytic anemia. The thoroughly washed red blood cells in this group of cases which are coated with an autoantibody of unknown origin, will be agglutinated by the Coombs reagent.

THE RH-HR FACTORS

As mentioned above, Rh− blood contains a genetically related factor known as Hr. In the Fisher terminology, all Rh factors are designated by capital letters D, C, or E, while the corresponding Hr factors are d, c, and e respectively.

The incidence of positive and negative reactions with each of the three sets of Rh-Hr factors are given in Table 6 along with other pertinent data.

As first shown by Levine, anti-C and anti-c give three types of reactions, because a type of blood (analogous to group 0) which has neither C nor c does not exist. As anticipated by Fisher, the same relationship holds for both D-d and E-e systems. It is because of this analogy to the serologic and genetic behavior of the M-N system that the letters in "Rh" were reversed to yield the term "Hr." Accordingly, the three types of bloods in any one system correspond to the three genotypes, e.g., DD (homozygous), Dd (heterozygous) and dd (homozygous).*

In each of the three sets, the difference between the positive for the one (Rh or Hr) and negative for the other (Hr or Rh) gives the incidence of the type heterozygous for both. Thus, in the case of the clinically important Dd factors, 85 − 37 or 63 − 15 = 48 per cent.

*As an analogy one may suggest the two genes which determine the three varieties of roses, red (homozygous), pink (heterozygous), and white (homozygous). A type containing neither the gene for red nor white does not exist.

TABLE 7

	Anti-D (Anti-Rh_0)	Anti-d (Anti-Hr_0)	Per Cent White Race	Incidence of Gene
DD homozygous	+	0	37	$\sqrt{37}=6.1$
Dd heterozygous	+	+	48	
dd homozygous	0	+	15	$\sqrt{15}=3.9$

The incidence of the three types and the two genes for the clinically important D-d (Rh_0-Hr_0) system are given in Table 7.

The incidence of gene *d*, which determines a negative reaction is the square root of the nonreactors or 15 per cent or 3.9. The incidence of the gene *D*, which determines a positive reaction, is 10 − 3.9 = 6.1.

Application of the binominal theorem yields the following results:

$DD + 2Dd + dd = (6.1)^2 + 2(6.1)\ (3.9) + (3.9)^2 = 100.$

DD or homozygous Rh+ = 37.
2*Dd* or heterozygous Rh+ = 48.
dd or homozygous Rh− = 15.

Similar calculations can be readily made for the C-c and the E-e systems.

OF THE six properties, the most important factor is D or Rh_0 and it is significant that this factor was described independently by Levine and Stetson in 1939 with the aid of an antibody (agglutinin) in a human serum and by Landsteiner and Wiener in 1940 with the aid of an experimental serum (rhesus blood injected into rabbits). The former workers dealt with a case of intragroup transfusion reaction due to transplacental transfer of fetal blood while the latter workers demon-

strated the heterogenetic relationship of a factor common to human or rhesus blood and hence the term "Rh."

Irrespective of the reactions with the five other Rh-Hr sera, the 85 per cent of individuals (white) whose blood contains the Rh factor will be designated as Rh+ while the remaining 15 per cent as Rh−. The data in Tables 2 and 6 indicate that the D factor (Rh_0) is at least 13 times more antigenic than the 5 other factors combined. This is all the more remarkable because there is greater opportunity for immunization against the factors d, E, C, and c. This is readily observed in a comparison of the incidence of the 6 kinds of incompatible matings (Table 6).

The four types of Rh+ and four types of Rh− individuals and their nomenclatures are given in order of their frequency in the white population of the United States.

So far as the clinician is concerned, the significance of these subtypes has been unnecessarily emphasized because the only diagnostic serum available for routine testing is anti-D (anti-Rh_0) and the use of this serum alone will detect at least 93 per cent of potential isoimmunization. For the protection of those Rh− individuals who may have produced anti-C as well as anti-D (87 per cent positive reactions), suitable compatability tests carried out with at least two random Rh− donors will be satisfactory. On the basis of their incidence, it is not likely that both Rh− bloods will belong to the rare types (6 or 8) which contain the C factor (see Table 8).

TABLE 8

Rh+	1.	DCe	Rh_1	54
	2.	DcE	Rh_2	15
	3.	DCE	Rh_1Rh_2	14
	4.	Dce	Rh_0	2
Rh−	5.	dce	rh	13.0
	6.	dCe	rh′	1.5
	7.	dcE	rh″	0.5
	8.	dCE	rh′rh″	very rare

Should anti-C and anti-E sera also be available, it is necessary to test only the Rh− donors and to exclude types 6, 7, and 8 as donors for immunized Rh− patients. They may safely be used, certainly at least once, for Rh− patients who have not been immunized.

The finer analysis of Rh+ individuals may be limited to husbands of Rh− women in order to determine their genotype and to prevent reactions in those rare instances (about 7 per cent) where Rh+ patients may have produced any one of the five other varieties of antibodies, either by themselves or in combination.

Unfortunately, the serum most useful for the direct determination of the genotype anti-d (anti-Hr_0) occurs very rarely so that it is necessary to resort to indirect methods. In brief, these are based on the frequency of certain gene combinations in the general population. Thus, an Rh+ individual of type Rh_1 is homozygous for the clinically important D factor if his blood fails to react with anti-c (anti-hr′). Thus, his genotype is represented as *CC* and on a statistical basis he is very likely also homozygous for D (i.e., genotype *DD*). Taking the three Rh-Hr factors into account, his genotype is *DCe/DCe*. This method will fail if the rare gene combination dCe is contributed by one parent.

Similarly, individuals of type Rh_1Rh_2 are, on a statistical basis, homozygous for the clinically important D factor because most frequently these individuals derive the Rh_1 antigens DCe from one of their parents and the Rh_2 antigens DcE from the other. The genotype is represented as DCe/DcE.

This indirect method cannot be applied to Rh+ individuals of type Rh_0 or Rh_2. In the absence of anti-d, valuable information may be obtained by testing the husband's parents and/or his children. If one of his parents or one of his children is Rh− he can be considered as heterozygous for D.

Were anti-d (anti-Hr_0) sera generally available for the differentiation of genotypes DD and Dd, the role of the other two Rh-Hr systems (C-c and E-e) would be far less significant for the obstetrician and general practitioner and their clinical application could then be limited to the finer study of the 7 per cent Rh+ mothers of affected infants or patients immunized by repeated transfusions.

ROUTINE MANAGEMENT OF OBSTETRIC CASES

The obstetrician and general practitioner are in an excellent position to allay the fears of Rh− patients created by unfavorable and inaccurate publicity in the lay press. As indicated above the vast majority of Rh− women will have two or more normal Rh+ infants before they produce antibodies.

The several steps in the management of these cases may be as follows:

1. Obtain a complete obstetric and transfusion

history, including also intramuscular injections.

2. Routine blood group Rh tests on all prenatal cases on the occasion of the first visit. There is no justification to omit these tests for primipara.

3. If the patient is Rh–, test the husband and children (if any) to aid in the determination of the husband's genotype, homozygous or heterozygous.

4. Test for the presence of antibodies in all pregnant women, Rh+ or Rh–.

5. Repeat the tests for antibodies in about the twenty-sixth, thirty-second, and thirty-seventh weeks of the pregnancy. All Rh– mothers should be retested about one to two months after the delivery of an Rh+ normal infant.

6. If there are no antibodies, the patient should be allowed to go into labor spontaneously. In the absence of antibodies in the postpartum specimen, another pregnancy may be recommended.

7. Labor may be induced a few weeks early if: (a) the patient's serum contains antibodies either from a previous transfusion or from a previously affected infant; (b) there is a sharp increase in antibodies in the thirtieth to thirty-sixth weeks; (c) the husband is presumed to be homozygous.

In no case should labor be induced so early that the factor of prematurity will be too great. In the event that the husband is heterozygous, one may still be justified in inducing labor if the first two conditions are satisfied. Even in the presence of an Rh– fetus, one may occasionally observe an increase in antibody content due to nonspecific stimuli of unknown origin.

The choice of procedure, induction or cesarean section, must be made by the obstetrician and cannot be influenced by the serologic findings.

8. In all cases, the cord blood should be tested with the Coombs reagent. If the Coombs test is strongly positive and a considerable quantity of maternal antibodies can be demonstrated in the infant's serum, a replacement transfusion should be carried out. As a rule, these conditions will be satisfied if the mother gives a history of a previous transfusion or delivered an affected infant.

In the vast majority of cases, however, the affected infant should recover with one or more simple transfusions (10 cc. per pound of body weight). The tendency has been to rely too much on the newer serologic tests which, however, may at times be misleading. It is, therefore, important to carry out time-honored physical examination of the infant and also to perform a complete hematologic study.

PROGNOSIS IN FUTURE PREGNANCIES

Once an Rh– woman has delivered an affected infant, the outlook is distinctly less favorable in future pregnancies with Rh+ fetuses. Excluding the very important role of previous transfusion, the vast majority of these Rh– women already have one or more normal Rh+ infants. Even if the husband is heterozygous, it is not possible to predict the Rh of the fetus in any given pregnancy except to state that there are 50 per cent chances for a normal Rh– infant.

In the present state of our knowledge, one is not justified in recommending another pregnancy with the hope that the next Rh+ infant can be successfully treated with replacement transfusions. More likely, the end result may be either intra-uterine fetal death, or recovery from the anemia with the after-effects of kernicterus.

Recently, Carter obtained extracts from Rh+ blood (hapten) which retain the property of neutralizing anti-Rh antibodies but have presumably lost their antigenicity (capacity to stimulate antibody formation). The implication is that strongly immunized patients will lose their antibodies if treated intensively with this hapten preparation. Although this biochemical approach to the subject is undoubtedly in the right direction, it is as yet premature to state that all hopes for a satisfactory therapeutic reagent have been fulfilled.

Too few patients have been tested over a sufficiently long period either during the course of the pregnancy or following a pregnancy with an affected infant. In the latter group, it is hoped that residual antibodies will be neutralized at a more rapid rate than the normal rate of diminution of antibodies in the postpartum period. This group of women can then be subjected to a more intensive therapy in the course of the next pregnancy. It has also been suggested by Carter that the hapten preparation could also be used in the therapy of the affected infant along with transfusions.

Unfortunately, the small yield of the active material makes it difficult to obtain a sufficiently large series of experimental cases. It would indeed be remarkable if the small quantities now available could effectively diminish the antibody content of a strongly immunized patient whose tissue spaces are saturated with antibodies. It is still to be estab-

lished that the hapten does not combine with tissue proteins and thus be converted into a full antigen.

There is no evidence to support the claims that ethylene disulfonate or vaccines early in the course of the pregnancy will inhibit antibody production. So far as vaccines are concerned, there are indications that their administration will stimulate isoimmunization.

In view of these circumstances, it is preferable to recommend that these women not be encouraged to attempt further pregnancies. As an alternative, one may suggest either artificial insemination with the sperm of a known Rh− donor or else adoption. Should an intensively immunized mother accidentally become pregnant, one is justified in recommending a therapeutic abortion provided that the husband is homozygous.

MECHANISM OF TRANSPLACENTAL TRANSFER

It is assumed that in every normal pregnancy a few fetal red blood cells find their way into the maternal circulation. It is significant that the Rh factor does not occur in a water-soluble form and it is probably limited to red blood cells, only small quantities of which are sufficient to induce immunization.

The intra-uterine passage probably begins in the latter half of the pregnancy when the fetal blood vessels become large and over an ever-expanding surface area, gradually approach the maternal sinuses from which they are then separated by a single layer of syncytial cells, aside from the endothelium. Other factors favoring the passage of fetal red blood cells are the sluggish circulation in the maternal sinuses and the greater pressure in the fetal circulation due to heart action and further increased by active fetal movements in the latter half of the pregnancy.

Additional evidence to indicate that there is no need to assume the existence of gross pathologic lesions in the placental villi will be found in the recent papers of Naeslund and Aren, Kline and Everett, and Henderson. One need not expect an absolutely impermeable barrier in an organ formed by the trophoblast, which like a malignant cell, is endowed with such invasive powers and rapid proliferation that in the course of a pregnancy it attains the tremendous contact surface area of 70 to 120 square feet required for the nourishment of the fetus. It has been calculated that when laid end to end the fetal villi in the term placenta exposed to maternal sinuses would attain a length of 11 miles.

The important role of transplacental transfer of fetal red blood cells is illustrated in those instances in which the firstborn infant is affected. In many instances there were no earlier abortions. These cases are a bearing on the subject irrespective of previous antigenic stimulation by intramuscular injection or transfusions. In the majority of the cases, the Rh− mother had been transfused in some instances as long as ten to fifteen years previously. The first appearance of antibodies in the latter third of the pregnancy can be interpreted only as the "anamnestic" response to antigenic material received from fetal blood in the course of the pregnancy.

NEW URINE TEST FOR PREGNANCY

A simple urine test for pregnancy which can be completed in one-half hour in the physician's laboratory has been reported by Dr. Garwood C. Richardson of Northwestern University. The Richardson test, based on the presence of a substantial amount of estrone in the urine, has been used on more than 1,000 cases over a period of five years and is called virtually 100 per cent accurate in diagnosis of pregnancy, even shortly after conception.

In the test, estrone is separated from progesterone derivatives by reaction of the urine to sodium hydroxide and chloroform. The ultimate sample for analysis rises to the top and is transferred to an inner test tube. Estrone in one procedure causes the sample to turn brown, indicating positive results; in another, it becomes violet-red. Estrone is acidic enough to react with sodium hydroxide to form sodium estronate. This salt is not soluble in chloroform and hence, if the solution containing it is extracted with chloroform, sodium estronate will remain in water solution. This solution then is caused to couple chemically with either of two reagents, each of which produces its typical color reaction diagnostic of pregnancy.

Surgical Treatment of Polyps of the Colon

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Polyps of the colon are of interest and importance largely because of their relationship to malignancy. I think it is not an unfair statement to make that of all the so-called precancerous lesions in the body, there is probably more definite proof that polyps of the colon are more likely to undergo malignant degenerative changes than lesions elsewhere.

Of course, we have all sorts of pathologic types from the fibroma to the lipoma, the papilloma, etc., but the polyps in which we are really interested as precancerous or important lesions are the adenomatous variety which occur as single polyps, as large groups of polyps, as polyps scattered throughout the various segments of the colon, or as definite, diffuse adenomatosis, polyposis, or whatever you choose to label that lesion, which I think should probably be called familial polyposis.

A single adenomatous polyp in the colon is of interest and importance largely in relationship to its location and symptomatology. In casual roentgenologic examinations of the colon, not infrequently one picks up polyps in various segments, either isolated or in some numbers. If they are any size, such as 1 or 2 cm. in diameter, and on a stalk, they are of sufficient significance to demand surgical intervention, even though one has to invade more than one segment of the large bowel.

If a single polyp, or two or three polyps, let us say, are viewed through a proctoscope, we have a different problem and one, which I think, is pretty readily solved, provided a definite pathologic diagnosis is made by specimen. I would insist on this specimen, if the polyp is in the rectum or lower sigmoid, necessitating radical removal—the whole polyp with a good deal of mucous membrane around its base; it is the mucous membrane around the base that the pathologist must examine to give you an idea of just what type of surgical approach you wish to make to this lesion.

I believe in the grading of polyps and the grading of all malignant tumors by the pathologist. In the case of a polyp of low grade removed from the rectum, if the specimens taken from the periphery of the polyp and from the base show no invasion and no malignant degeneration, a simple excision may be all that is necessary. However, if a polyp has invaded the mucous membrane around the base, one has to do the same type of operation as for a higher grade cancer of the rectum.

That gives me the opportunity to say that I still believe that high grade cancers of the rectum, most of which develop on polyps, should be treated radically. I am sure Dr. Buie told you earlier in the meeting* that polyps and cancers of the lower bowel occur in the same anatomic locations in practically the same percentage of cases; that is, about 70 per cent of the polyps occur in the sigmoid and the rectum and about 71 per cent of the carcinomas of the colon and rectum occur in the same location. I think there is no question that the vast majority of these cases develop in polyps,

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*Buie, Louis A.: Polypoid disease of the colon. Postgrad. Med. 5:3, 177 (March) 1949.

and what better proof could one have than the familial polyposis which, in practically every instance—unless treated radically by surgery—ultimately develops malignancy and causes the death of the patient.

This diffuse polyposis or adenomatosis of the colon, this familial polyposis, should be definitely differentiated from the pseudopolyposis which follows inflammatory diseases, particularly chronic ulcerative colitis in the large bowel. I think that Bargen has estimated that between 5 and 10 per cent of the chronic ulcerative colitis cases develop pseudopolyps, and of those polyps, more than an occasional one undergoes malignant degeneration. However, in the familial type, the true adenomatosis, which may be present throughout the entire colon or invade only segments of the colon, malignant changes invariably result if the individual lives long enough.

The first case of diffuse polyposis or adenomatosis was described as far back as 1721 by Mendel. It was a pathologic specimen, of course, and later in about 1839 Rokitansky reviewed what literature there was and reported on some more cases of polyposis. It remained for Dukes in this century, however, and Cripps, to bring us up to date on this subject, for in 1882 Cripps reported two cases of his own and reviewed the literature; he was the first man to call attention to the familial type of this disease.

The reason I think that we feel we can prove this type of ailment results in malignancy is the work of quite a few investigators. Wexelman first, before 1900, used as his criteria changes in the epithelium of these polyps, and subsequently Hauser and Westhaus added connective tissue changes in the microscopic picture (that was in the 1920's) which showed definitely the progression from benignancy to malignancy. There is no question, at least in my mind, that this has been established beyond a doubt.

In 1931 with Fitzgibbon I reported 13 cases of familial polyposis which had produced 24 carcinomas in all. These polyps we divide into three phases. There is Group I, which never undergoes malignant degeneration, in which all of the epithelial structures have differentiated into normal mucosal patterns, and there may be or may not be a stalk. I can conceive of few better opportunities to prove the traumatic theory of cancer production than in a polyp, because the fact of the constant tug on the mucous membrane of these

FRED W. RANKIN

polyps by the peristaltic action of the bowel, in addition to the trauma of the fecal current in the left side of the colon, seems to me to add a great deal of weight to the argument.

A sessile polyp of the Group I variety in which there are no epithelial changes whatsoever is shown in Figure 1. The whole thing has differentiated perfectly normally, and that polyp never undergoes degeneration into malignancy.

FIGURE 2 illustrates how the high-power microscopic picture shows widespread failure of the epithelium to differentiate into normal mucosa. The cells are hypertrophied, elongated, and filled into buds which project into the lumen of the tubules, and the proliferation is irregular and without mucous formation. The stalk is being formed, and the longer this polyp exists in the colon and the more the peristalsis tugs at it, the longer the stalk will be pulled out. These polyps become very good sized—from 3 or 4 mm. up to 2 or 3 cm. in diameter—and occasionally they are broken off and discharged per rectum because of the action or trauma of the bowel content and peristaltic pull.

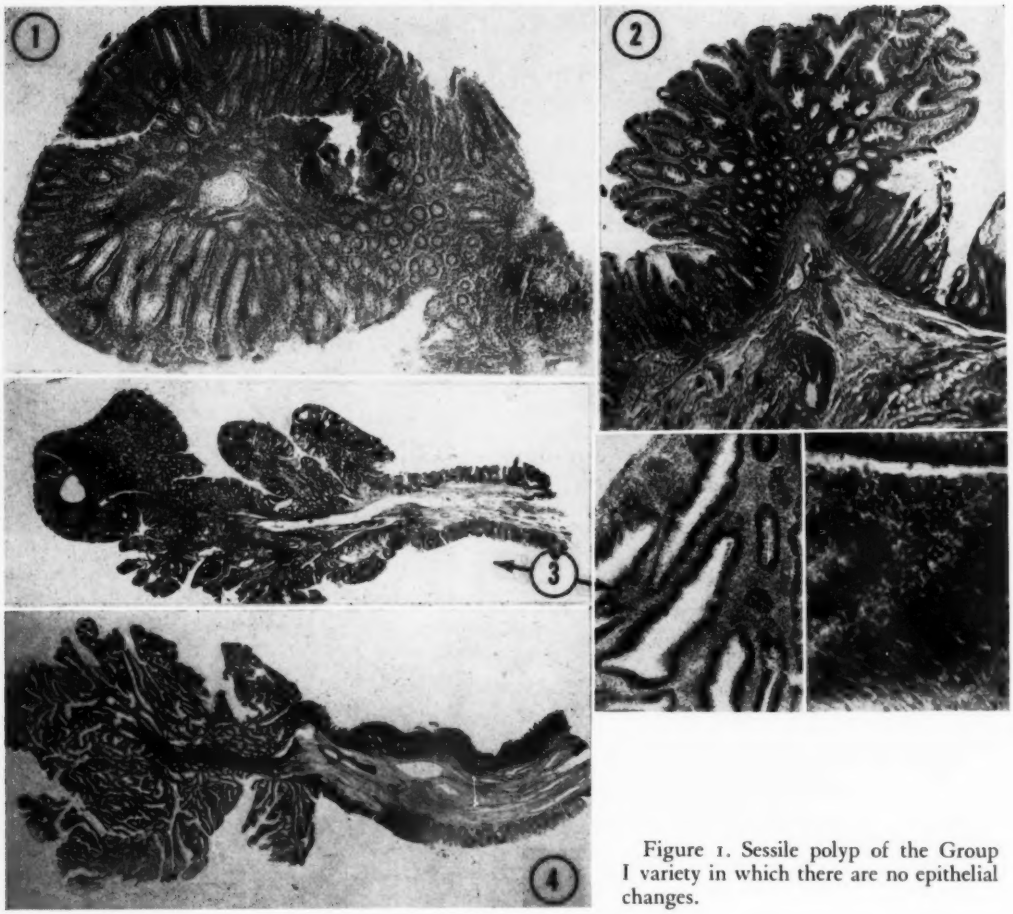

Figure 1. Sessile polyp of the Group I variety in which there are no epithelial changes.

Figure 2. High-power microscopic view showing widespread failure of the epithelium to differentiate into normal mucosa. Cells are hypertrophied, elongated, and filled into buds which project into the lumen of the tubules, and proliferation is irregular.

Figure 3. Group II polyps which differ but little from those of Group III.

Figure 4. Carcinoma developing in a polyp. The carcinoma is seen in the upper and outer margins.

These look like big adenomatous polyps; they look papillomatous; they are shaggy in appearance, and grow into the lumen of the bowel. This is the kind of polyp to undergo degeneration in so far as the prognosis is concerned. I do not know what wise old surgeon said that a cancer which grows away from you has a better prognosis than one which grows to you, meaning that a sessile lesion which is growing toward the mesentery of the bowel is liable to be more malignant and to metastasize earlier than a polyp which is projecting into the lumen and therefore growing away from you.

There is very little difference between Group II and Group III polyps (Figure 3). The polyps of Group II are just a little more formed, with a little more connective tissue being drawn into the stem. The Group III polyps are small and very

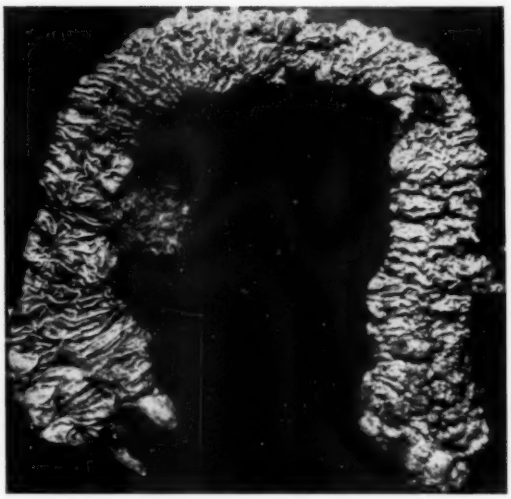

Figure 5. Typical polyposis of the colon.

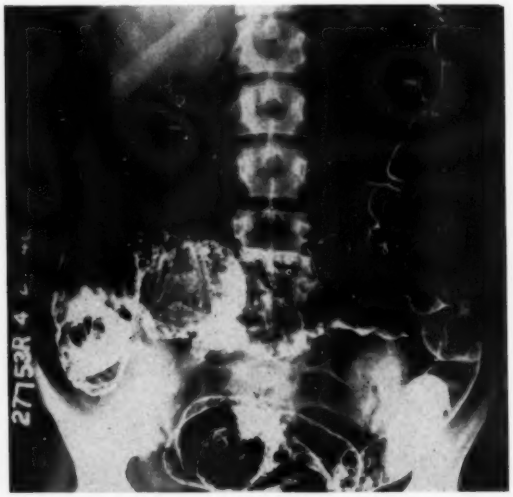

Figure 6. Diffuse polyposis in patient whose brother also had diffuse polyposis throughout the colon.

cellular, with the tree-like stalk characteristic of them. These tumors are smaller than Group II. They are usually more sessile, proliferate very rapidly, and have very little if any connective tissue in the stroma.

We may not all agree, but I think that I would insist that this type of tumor does undergo malignant degeneration, and when it fills the whole colon we have a lesion which must be dealt with surgically and radically.

Carcinoma developing in a polyp is shown in Figure 4. The carcinoma is seen in the upper and outer margins. A typical instance of a polyposis of the colon may be seen in Figure 5.

Figure 6 illustrates a case in which the patient is a brother of a man who is one of the doctors here now. The latter (the doctor) came to me when he was 15 years of age with polyposis symptoms of only four months' duration; the symptoms consisted of bleeding. Examination showed diffuse polyposis throughout the colon. The father had died of carcinoma of the rectum at the age of 37 or 39. His brother was examined after his operation and found to have diffuse polyposis too. I did a colostomy on him because when I explored him to do an ileostomy and subsequently remove the colon, I found such a large bunch of polyps down in the lower sigmoid that it was impossible to do it without further fulguration. The polyp extruded itself some days later. He had a number of those polyps down into the lower loop, which was subsequently cleared. This man was 24 years old at the time.

A colon which was removed, showing the most diffuse type of polyposis is seen in Figure 7. You would think that in as large a tumor as that you would have malignant degeneration. Actually we did not find any malignant degeneration in any of these polyps that were examined microscopically, and a good many of them were gone over. That is just like the nap on a carpet; wherever you look there are polyps, and this involves the whole colon.

Figure 8 is a roentgenogram of a man 34 years of age who has diffuse polyposis. You see it everywhere. There is a cancer of the hepatic flexure and a cancer near his splenic flexure. Strangely enough, he had had symptoms for a very short while. The symptoms consisted of bleeding, depletion, and so on. He came up for examination, and a diagnosis of polyposis was made with two cancers in his colon. That was subsequently proven correct. Although he had a little difficulty with his early fulguration because we went a little high and he had a slow leakage which had to be re-treated and walled off, subsequently he was satisfactorily operated, with an ileocolostomy, and the whole colon

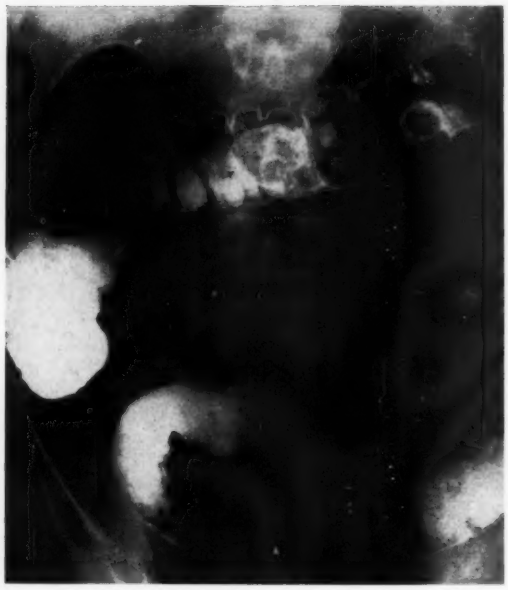

Figure 7. Colon showing the most diffuse type of polyposis.

Figure 8. Diffuse polyposis in male patient, 34 years of age. There is a cancer of the hepatic flexure and a cancer near the splenic flexure.

Figure 9. Roentgenogram of sister of patient in Figure 8, showing many polyps throughout the colon.

removed. It is two years since I did this, and he is in good health.

His sister, who came with him, had had no symptoms (Figure 9). These two cases are similar to the two young men I spoke about. She has many polyps all around throughout her colon. I operated in the same manner, an ileocolostomy and subsequently colectomy, and she did satisfactorily likewise.

Figure 10 shows the incidence of symptoms in 10 cases. There was bleeding in most of them. The oldest man was 34, the youngest 15. Many of these cases are younger than 15, but it is rare to have anyone over 30 years of age without symptoms which have called for an examination. Eight cases had bleeding; 5 had cramps; 4 had diarrhea; 1 had tenesmus; 2 were asymptomatic—these were the brother and sister whom I examined without having had any symptoms whatever.

The symptoms had been present for less than six months in 3 cases, less than a year in 1, over five years in 4, and there were 2 asymptomatic

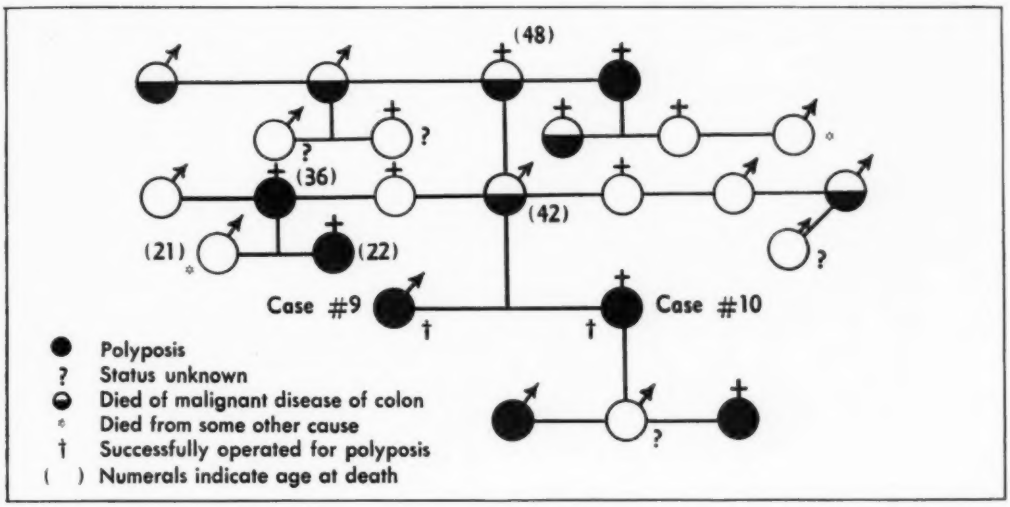

Figure 10. Incidence of symptoms in 10 cases.

cases who were 32 and 34 years of age, so you see how materially it varies.

The trend in surgical treatment as I have followed it through this small series is given in Table

TABLE 1

TRENDS IN SURGICAL TREATMENT

YEAR	CASE NO.	METHOD
1932	1	Ileostomy, subtotal colectomy, proctectomy
1934	2	Ileostomy, subtotal colectomy
1935	3 and 4	Ileostomy, subtotal colectomy, ileosigmoidostomy, fulguration
1937	5 and 6	Fulguration, ileosigmoidostomy, subtotal colectomy
1939	7	Cecostomy (elsewhere), fulguration, ileosigmoidostomy, subtotal colectomy
1940	8	Fulguration, colostomy, ileosigmoidostomy, subtotal colectomy
1947	9 and 10	Fulguration, ileosigmoidostomy, subtotal colectomy
1948	(?)	Total colectomy, anal ileostomy (Ravitch)

1. In the first few cases we did ileostomies, then subtotal colectomies, and a proctectomy. I think we have turned that all around, and I believe we do much better than before. Even if there is a question of malignancy, I think the idea ought to be to save the sphincteric mechanism and clear out the rectum by fulguration and then do an ileosigmoidostomy, and subsequently do colectomy as a second stage. An ileostomy is a very unhappy companion. A colostomy is easily borne. There is a great difference in which one you have to tolerate, and I should advise against an ileostomy any time it can be avoided. First clear out the rectum; second, do the ileosigmoidostomy; third, do the colectomy, and remember that the patient must be investigated every three to six months by proctoscope to see if there are any recurring polyps.

One thing I would like to mention in closing. In 1948 a very brilliant young surgeon down at Hopkins, Ravitch, after doing a good deal of experimental work, reported a successful case of ileostomy, saving the rectal sphincter and bringing the ileostomy out through the rectum. I believe in this type of case it perhaps should be considered. For myself, I have not done it. I like the other way, but it is something that I think could be considered very definitely in the treatment of chronic ulcerative colitis if the lower part of the rectum and the sphincteric mechanism are not too much involved.

I do believe that polyposis of the colon is best treated by radical surgery done in two stages following fulguration of the polyps from the rectum, and I think it is definitely important that it be treated as early as one possibly can do so.

DIAGNOSTIC CLINIC

Diagnosis and Treatment of Bronchiectasis

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THROUGH the kindness of Dr. Kaye I am going to review with you the histories of 3 patients from his clinic.

The first patient is a young man 18 years of age who has had productive cough for five years. One year ago he developed empyema, which was drained at that time.

The next patient, a young lady of 25, has had cough and sputum since an attack of pneumonia at the age of 3. Associated with her cough and sputum have been recurrent hemorrhages, many of them severe. The sputum has been chunky in character, foul, and amounted to one cupful daily.

The third patient, a young man of 21, has had chronic productive cough all his life, many attacks of pneumonia, and one cupful of sputum daily.

Let us analyze that symptomatology, because these 3 patients illustrate pretty well the story of bronchiectasis. That symptomatology is chronic cough and sputum. The cough is paroxysmal in character. It is influenced by posture and therefore is most likely to appear in the early morning or when the patient leans over. The sputum is usually, but not always, foul. It frequently is streaked with blood and often there is gross hemoptysis.

There is a small group of patients whose only symptom is that of recurring hemoptysis. It is interesting that in my experience many of these patients have not had very extensive disease.

These 3 patients have illustrated the recurring pneumonia that results from interference with drainage and the subsequent extension of bronchopneumonia in the diseased area of the lung. Accompanying that pneumonia, there is often pleurisy; if the pleurae become adherent, the pleurisy is likely to disappear.

A small number of patients have shortness of breath—only those, as a rule, with extensive or long-standing disease and secondary changes in the remainder of the lung.

PHYSICAL SIGNS

Some patients show all the signs and symptoms that one would anticipate. They have diminished movement of the involved side of the chest; there is lessened air entry and dullness; there are râles, usually medium sized and large. But the thing to remember particularly about patients with bronchiectasis is that many of them show no alteration whatever in physical signs, and I think that fact is one of the greatest sources of error. One is likely to be led astray and think that because there is no alteration in physical signs, the patient does not have serious disease.

Clubbing of the fingers is a common sign. Why this is present in one case and not in another has not been explained satisfactorily, however.

DIFFERENTIAL DIAGNOSIS

What would have been the differential diagnosis in patients such as those presented? Of course one thinks first about the possibility of tuberculosis, and that should always be excluded. Every patient

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should have a careful examination of the sputum for tubercle bacilli whether or not one really suspects it, because occasionally, even in lower lobe disease, one will be surprised to find that the disease has an underlying tuberculous origin.

Such symptomatology could be produced by a chronic lung abscess. The history of onset is usually different, however, and a thorough investigation will usually rule it out without difficulty.

The first young man presented had empyema, a common complication in bronchiectasis. The pathology is not difficult to imagine; it is due to the development of a small subpleural abscess which ruptures into the pleural cavity.

For patients in the older age groups, the diagnosis of adenoma of the bronchus or carcinoma of the bronchus with a complicating infection beyond an obstruction must be considered. It is a good rule that patients of 40 years of age and older developing cough and sputum of this nature, should be considered to have a new growth of the bronchus until it has been excluded. They might have a stenosis of the bronchus with an infection beyond the point of obstruction. Most stenoses of the bronchus are tuberculous in origin—not quite all.

Following a thorough clinical investigation, the next thing to do is have a plain x-ray plate of the chest. This will usually exclude tuberculosis and chronic lung abscess. It may be a bronchiectasis which has arisen in an abscess, and this must be determined.

The next thing to do is to have bronchograms made, with lipiodol injection into the involved area of the lung. The most common reason for an unsatisfactory result following operation is imperfect mapping of the lung before surgery.

In addition to the P-A film, the lateral film, and the oblique film, we have found it desirable to take spot films, much as is done in gastrointestinal diagnosis. In this way we are perfectly certain that we have visualized every division of the bronchus and after analyzing this series of films, we know without question the extent of the patient's disease.

ROBERT M. JANES

THERE is one more investigation that should be carried out in every patient, namely a bronchoscopic examination. In most of these patients one would not expect that it would reveal much that would aid in the management of the patient, but the possibility that there is an underlying pathologic change in the bronchus as the primary factor must always be considered. It must be remembered, particularly in those patients who have developed the disease in their second decade or later in life, that they may have a foreign body in the bronchus. We have been astounded on several occasions to find a totally unsuspected foreign body as the etiologic factor. Every patient, therefore, should be bronchoscoped before surgical measures are undertaken.

TREATMENT

What can medicine offer these patients in the way of treatment? It can offer nothing but palliation. It should not be dismissed, however, particularly in those patients who have disease that is too extensive to permit surgical procedures; a conscientious postural drainage, perhaps associated with the use of antibiotics, may make that patient's life supportable whereas previous to treatment it was not worth while. It is really amazing how relatively comfortable some of these patients with extensive bilateral disease can be made if one can induce them to sleep each night with the head 15

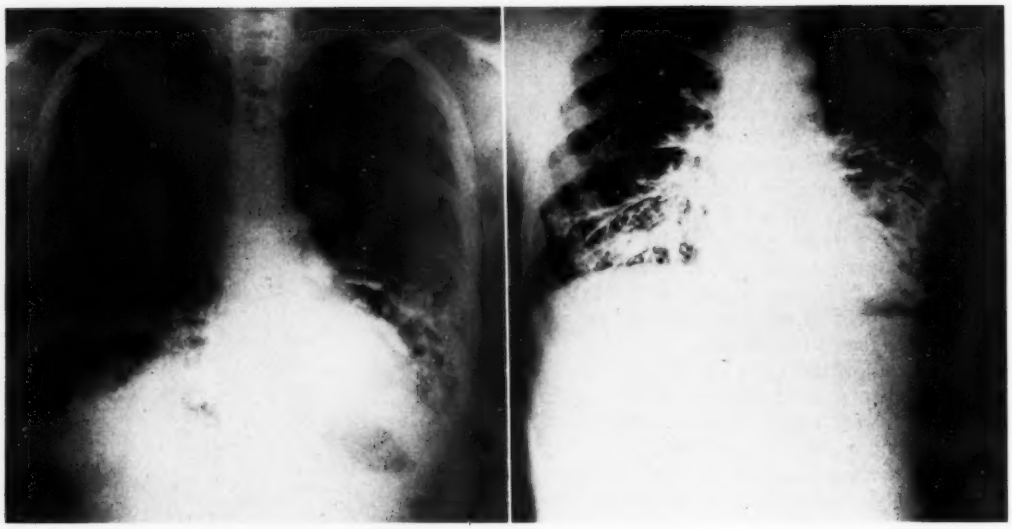


Figure 1. Unsatisfactory bronchograms. A (left). 1931—left lower lobe and lingual process involved. B (right). 1935—left lower lobe and probably lingual process involved.

to 18 inches lower than their feet, and in addition, if postural drainage is carried out once or twice during the day.

In which group of patients is surgery most likely to be satisfactory? What extent of lung can one remove? One can remove, of course, either the lower lobe, the lower lobe and lingula, the lower lobe and middle lobe, the middle lobe alone, or one entire lung. This always reminds me of one of our most grateful patients who had the whole of one lung removed a good many years ago. He is so grateful because his occupation is that of housebreaker and he no longer disturbs the occupants.

One can remove one upper lobe and one lower lobe and even go so far, as has been done in one of these patients, as to remove both lower lobes, the lingula, and the middle lobe.

The latter resection can be done with reasonable prospect of success in patients under 40 years of age; as the patient passes the age of 30, however, one must look upon him with closer and closer scrutiny, because he may have developed secondary fibrotic changes in the remaining apparently normal lung which will interfere with the result. I think extensive bilateral resections are very doubtful in patients over 30 years of age and we hesitate to do them except in exceptional circumstances.

Progress in the surgical management of bronchiectasis, so far as mortality rates are concerned, has been better than any of us engaged in this work at the beginning could have hoped for. The mortality rate in unilateral resection is not more than 2 per cent. Many series have been reported in which the mortality rate has been a fraction of 1 per cent. It must be remembered that for the most part these very good figures have come from hospitals where soldiers were being treated. The patients were young, formerly healthy men, and are unlikely to be duplicated in an ordinary series of patients seen in adult hospitals.

Our results, as far as mortality rates are concerned, are sufficiently good that we as surgeons can now afford to admit some of our shortcomings, and it is time that we began to consider why our results are not all satisfactory.

In the ordinary series of patients, about 70 per cent of results are almost completely satisfactory. The reasons for unsatisfactory results in the

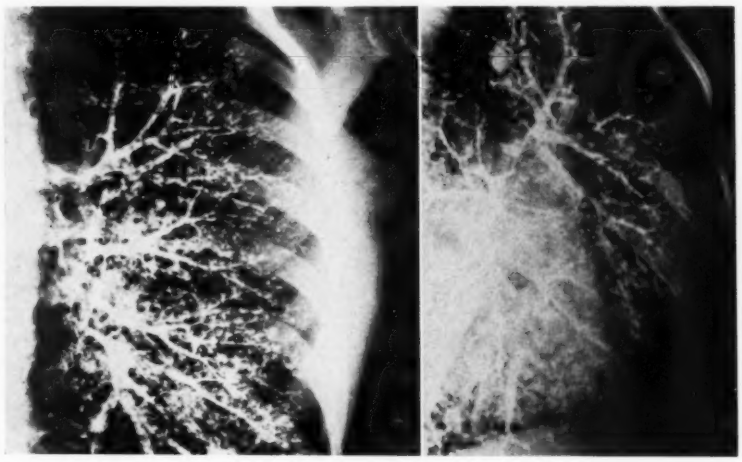
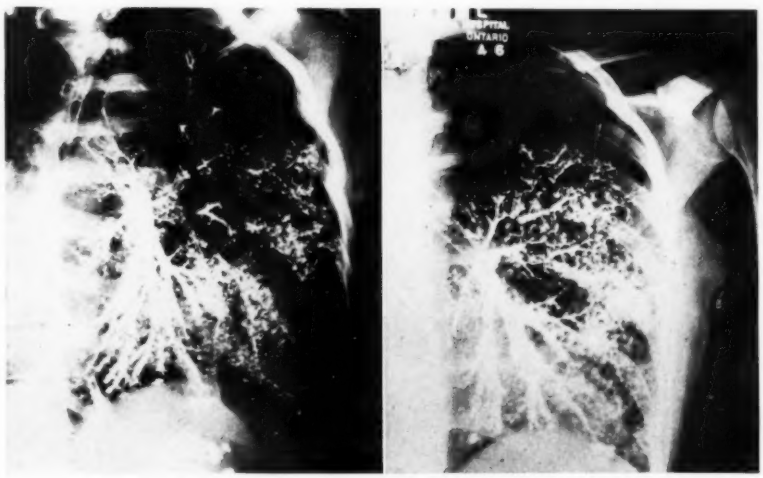


Figure 2. Satisfactory filling—conventional PA and L films. A (above). Right side—normal. B (below). Left side—lower lobe involved.



remaining cases are first, incomplete localization of the disease, and therefore the leaving behind of an area of bronchiectatic lung. In such a case, the patient will continue to have cough and sputum, though probably to a lesser degree, associated hemorrhage, and many of the disabilities that existed before treatment.

I think the next most common reason for unsatisfactory results is chronic sinusitis. While it is not a contraindication to operation, these patients

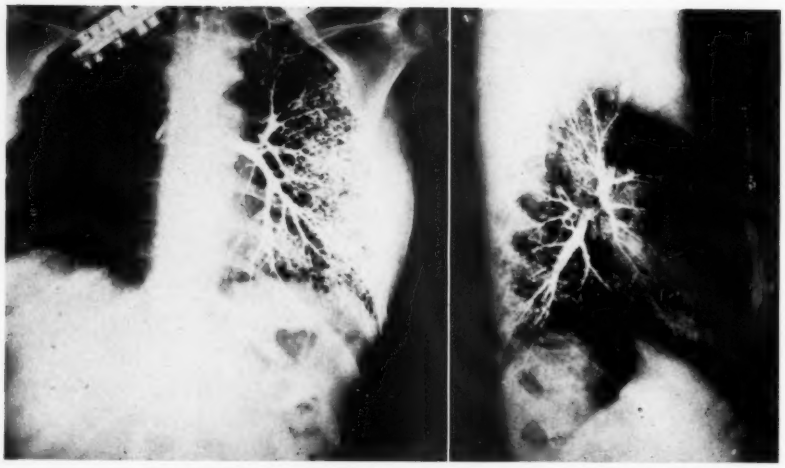
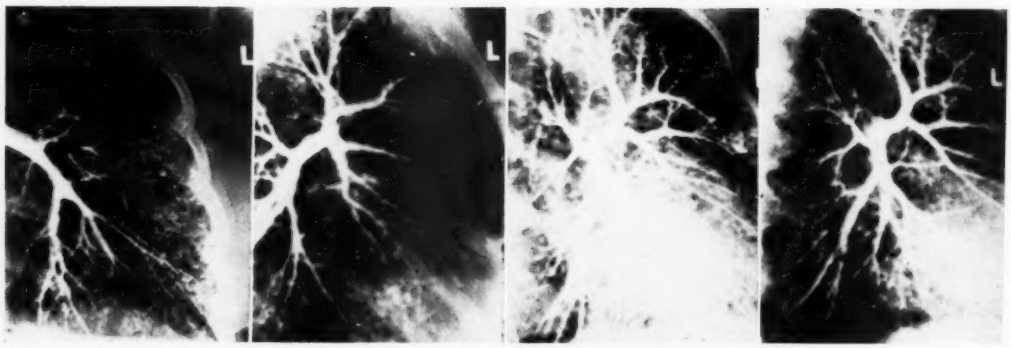


Figure 3. Bronchograms of normal bronchial tree. A. Conventional PA and L films.



B. Spot films bring each branch into relief.

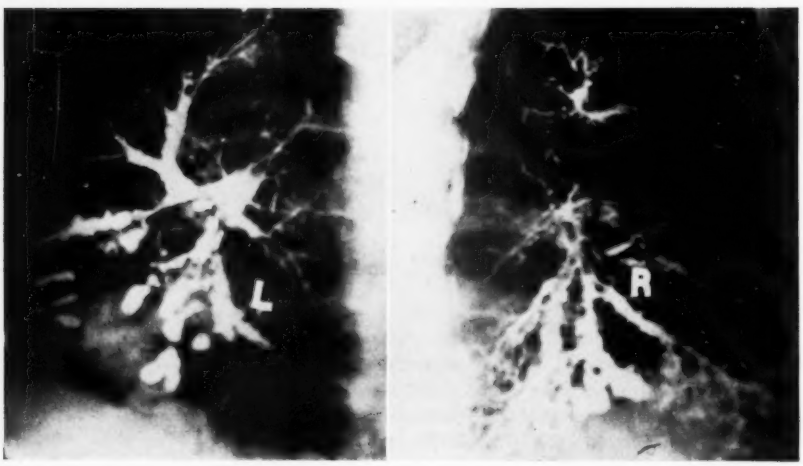


Figure 4. Spot films of patient with bilateral disease.

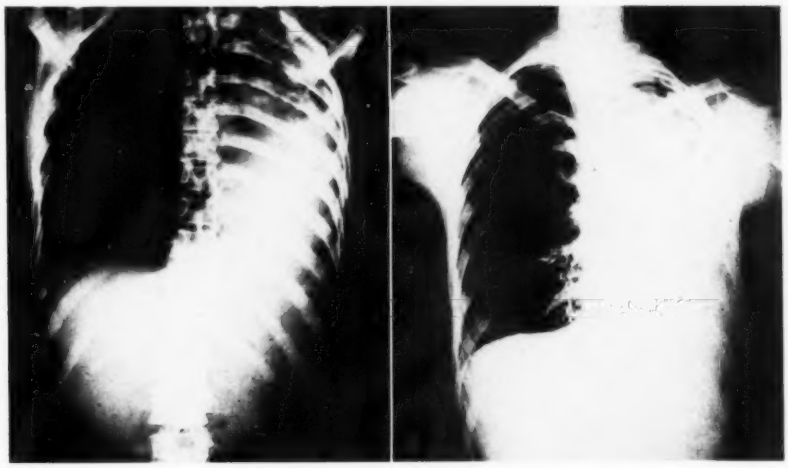


Figure 5. Tuberculous bronchostenosis with secondary bronchiectasis—poor filling due to obstruction of the bronchus.

will continue to have some cough and sputum.

Increasing age mitigates the results. Considerable degrees of fibrosis can be present in the remaining lung without being recognized in the x-ray, and one has to examine carefully any shortness of breath. Vital capacities should be done and, of course, ideally, a bronchospirometer should be used to measure the vital capacity of the remaining good lung.

In my experience, I have found that patients with asthma are not cured by resecting the bronchiectatic area of the lung. They will, of course, be rid of much of their sputum and will be improved, but they will still have their asthma. In those cases that have developed fibrotic changes in the remaining lung as a result of long-standing disease, the patients may actually be worse as a result of resecting the bronchiectatic area which may have been taking some part in ventilation.

The patients presented today illustrate reasonably well the results that may be obtained in certain groups of cases. The young man I spoke of first who had empyema as a complication, showed involvement only of the left lower lobe when bronchograms were made. He has been rid of nearly all his sputum, but he has chronic sinusitis and some morning cough. His result may be expected to improve with time.

When bronchograms were made of the next patient, she was shown to have involvement of the right lower lobe, the left lower lobe, and lingula. She was operated on August 13, 1948, the right lower lobe being removed. She is rid of about half of her cough and sputum, feels much better, and is able to carry on her work as a bookkeeper. It is, of course, contemplated that she will

Figure 6. Carcinoma of the bronchus with secondary atelectasis and bronchiectasis.

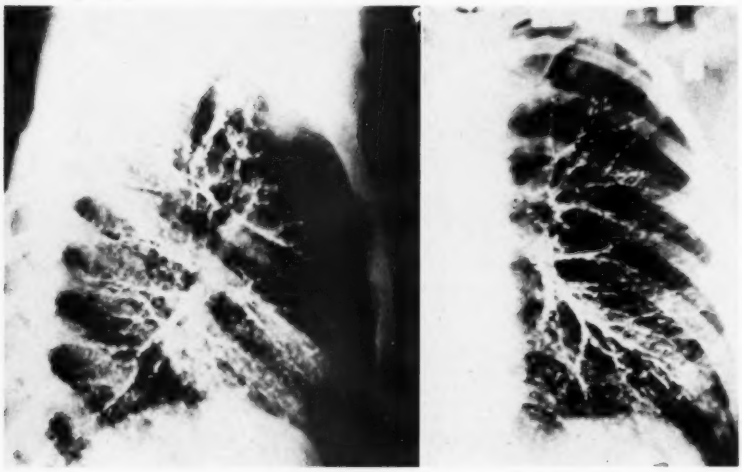
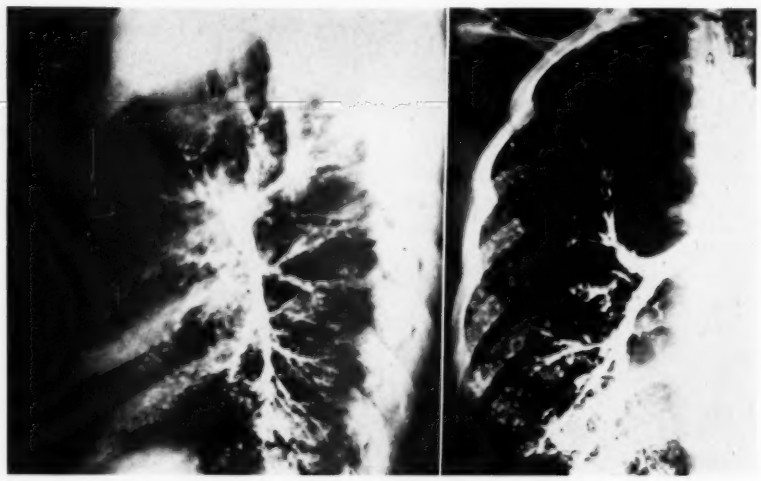


Figure 7. Patient's history and physical findings consistent with bronchiectasis yet bronchograms normal. A (above). Right side. B (below). Left side.



have a removal of the remaining diseased lung, perhaps a year after the first operation. She is much improved, but she is not cured.

The third patient, the young man who had chronic cough all his life, many attacks of pneumonia, and one cupful of sputum daily, had involvement of the right lower lobe, the left lower lobe, and lingula. The left lower lobe and lingula were removed May 12, 1947; the right middle lobe, together with a segmental resection of the right lower lobe, January 7, 1948. I have not had a chance to question him as to how well he is, but

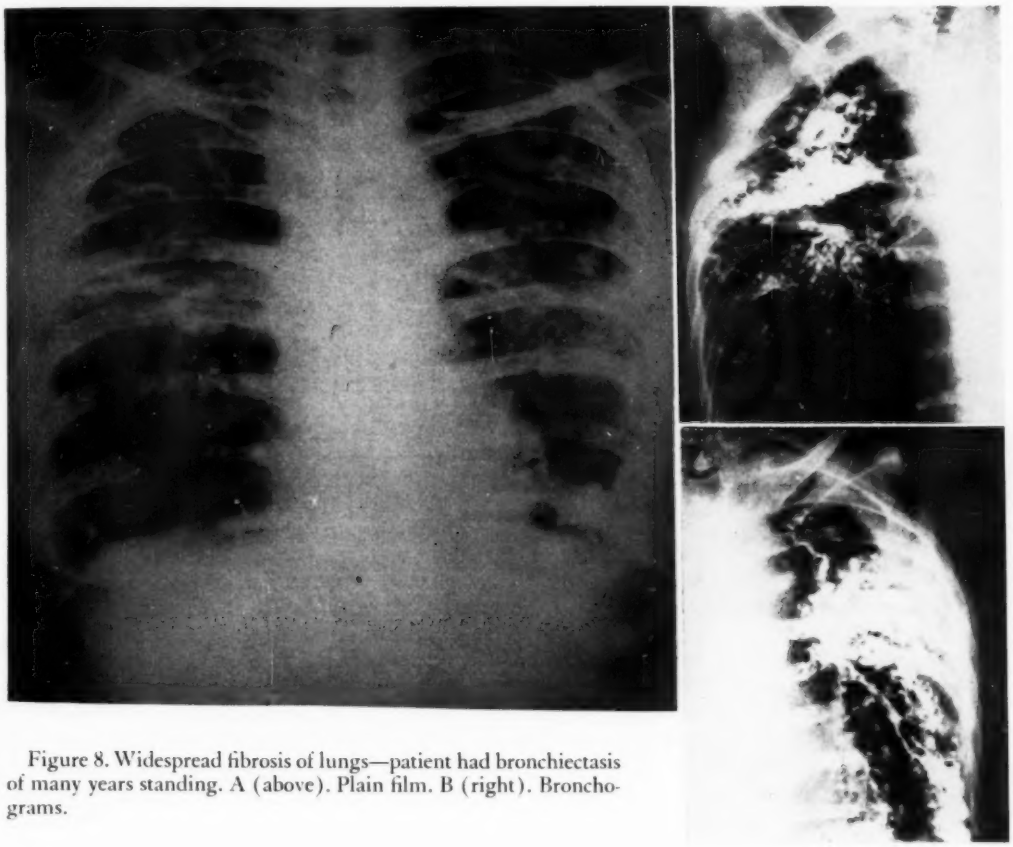


Figure 8. Widespread fibrosis of lungs—patient had bronchiectasis of many years standing. A (above). Plain film. B (right). Bronchograms.

when I was looking for him he had disappeared among the audience to listen to the papers we present, so I take it that he is reasonably well. Is that so?

PATIENT: Yes, sir.

DR. JANES: Have you any cough or sputum?

PATIENT: No.

DR. JANES: Are you short of breath?

PATIENT: No.

DR. JANES: What do you do?

PATIENT: I work in a beverage store.

DR. JANES: I think these excellent results that Dr. Kaye has presented to us illustrate relatively well what may be accomplished by surgery. Only in the cases that are not suitable for surgery should one be content with medical measures. The results, if one is careful in his selections, are among the most brilliant in the whole field of surgery.

DIAGNOSTIC CLINIC

Diagnosis and Treatment of Cirrhosis of the Liver

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WHAT is this disease called cirrhosis of the liver? Cirrhosis of the liver is a chronic, diffuse, progressive fibrosis of the liver, preceded or accompanied by more or less fatty infiltration. The prognosis in this disease is generally poor, but has been distinctly improved by recent advances in therapy.

The chief cause of cirrhosis of the liver is dietary inadequacy. In this country, or at least in California, chronic alcoholism is the principal cause of this inadequate diet. Lack of sufficient protein foods is the primary reason for liver damage in this disease. Why it develops in only a small percentage of the undernourished and chronic alcoholics is unknown.

Pathologically, cirrhosis of the liver is the advanced stage of a chronic, widespread damage to the liver cells, as evidenced by (1) more or less fatty infiltration within the liver cells, and (2) a varying amount of periportal fibrosis.

Physiologically, this diffuse fatty infiltration and portal fibrosis results in a varying degree of (1) liver failure, and (2) portal hypertension. The liver failure results from interference with the functioning of large numbers of the liver cells or actual destruction of these liver cells. The portal hypertension results from obstruction to the flow of the portal circulation, not only from the increasing fibrosis with distortion of the liver lobule, but from the distention of the liver cells by the fatty infiltration. Portal hypertension also results from more or less shunting of the blood from the hepatic artery to the portal circulation. This shunt produces arterial pressure effects in the portal system.

Clinically, the liver failure and portal hypertension are responsible for the ascites, hematemesis, enlarged liver, and other signs and symptoms so characteristic of this disease.

The term "cirrhosis" is in general synonymous with such names as Laennec's cirrhosis, portal cirrhosis, atrophic cirrhosis, alcoholic cirrhosis, hobnail liver, and diffuse hepatic fibrosis. It is probable that Banti's syndrome, or congestive splenomegaly, is also a synonym. All of these terms have defects because we do not know the etiology. For instance, they are not all atrophic; in fact, most of them have large livers. It is not alcoholic cirrhosis, because alcohol alone cannot produce cirrhosis; there must be a dietary inadequacy along with it.

Laennec's cirrhosis is probably as good a term as any but in general eponyms are not desirable. We hope we will have a more descriptive term. Chronic diffuse hepatic fibrosis is probably the best we can do at the present time. Laennec in 1826 had trouble naming this disease. He objected to the use of the word "scirrhous," meaning hard, which was popular at that time as a designation of this disease, and substituted the word "cirrhosis," which means merely orange-colored, from the Greek word "kirrhos." This particular change in terms did not advance our knowledge, as most of us still regard cirrhosis as referring to a hard liver rather than to an orange-colored liver. At present,

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cirrhosis is the name commonly used to describe a chronic, usually progressive, fibrous hepatitis, preceded or accompanied by fatty infiltration.

The average case of cirrhosis of the liver, like the one presented for discussion here, comes in for study and treatment in the far-advanced or decompensated stage.

The patient we wish to present is a 57-year-old white male. The excellent summary of his case was provided for me by Dr. Van Noate, and I greatly appreciate it.

CASE REPORT

Five years prior to admission to the hospital, the patient had been told that he had liver trouble, but had done nothing about it. Three months prior to admission there was noted a progressive swelling of the abdomen, and one month prior to admission there was noted the onset of constipation, acholic stools, dark urine, and swelling of the feet. There was no history of jaundice, hematemesis, or melena. There had been a weight gain of 17 pounds in the five months prior to admission. The past history was significant in that the patient had been a chronic alcoholic for approximately seven years, consuming on the average of ten to fifteen shots of whiskey and fifteen to twenty bottles of beer a day. During this period of time the dietary intake was poor. System review was essentially negative.

W. PHILIP CORR

LET us discuss the summary of this case.

The patient's age of 57 is a common age for cirrhosis of the liver. Sixty per cent of these cases are between 40 and 60 years of age. Eighty per cent of them occur after 35 years of age. It may, however, occur at any age. In countries where there is considerable malnutrition even children often develop cirrhosis. Over 70 per cent of cirrhotics are men, probably because men drink more alcohol, but women are fast catching up.

Liver trouble was definitely diagnosed in this patient five years previously and at that time he was told to stop his use of alcohol. One might say that we have, in this case, a five-year cure although he kept on taking his alcohol and kept on his deficient diet all during this period.

He has had swelling of the abdomen for three months. This swelling is due to ascites, as you can well see. He has a very nice fluid wave. After he gets rid of his fluid, they tell me that his liver is definitely palpable. He has an abdominal paracentesis every two weeks. He has a fetor hepaticus. At present he is mildly jaundiced. He has some good spider nevi in the region of the superior vena cava, as is common. He has one on his face, and I notice some on his hands. When he first came in palmar erythema was noticed. He did not have gynecomastia.

Spider nevi, palmar erythema, and gynecomastia are among those things which are probably due to the inability of the liver to destroy the supply of estrogens that are constantly being formed even in men. These estrogens sometimes accumulate so much that men lose their hair on their bodies and in their axillae. This patient has not lost any hair. This patient has edema. The story is that he had edema coming on a month before he entered the hospital and that he had ascites developing three months before he entered the hospital.

I asked him what symptoms he first noticed, and he said swelling of the ankles, which is rather common. He had pitting edema. He does not have nearly so much now as he had before, but it has been severe enough so that there was pitting up above his knees.

He is a chronic alcoholic of seven years' duration. Ratnoff and Patek stated that a chronic alcoholic was one who drank daily at least 6 ounces of whiskey (this man has had 10 or 15 "shots," which would probably qualify him) or 6 bottles of beer (this man has taken 15 to 20 bottles daily) or a quart of wine. There are all sorts of definitions for chronic

alcoholics but this one will do. Most of the patients far exceed this minimum, as this one did.

His dietary intake was poor, according to his own admission. He said his appetite was poor. Alcohol provides so many calories these patients do not feel like eating very much, and often they do not eat the proper proteins.

The physical examination on admission to the hospital revealed a man who appeared acutely ill. There was a slight icterus of the skin and sclerae. A rectal examination was carried out. His blood work was essentially negative. He had a low blood non-protein nitrogen of 22 mg. per 100 cc., which is a common finding. The serum proteins were down some, but his serum albumin was particularly low—1.6 gm. per 100 cc. with the normal being around 4.4. These patients will develop edema of the legs and ascites when it gets down somewhere below 3.5 gm. per 100 cc., and this man's serum albumin is well below that.

The prothrombin time was 41 per cent of normal. If this low prothrombin time should persist after the use of vitamin K one can be quite sure that there is severe liver damage. These patients may bleed from the mouth, the gums, or into any skin or mucous membrane area if the prothrombin time goes below 10 per cent of normal. His serum icterus was 34, which made him definitely jaundiced. His bromsulfalein test revealed 32 per cent retention of dye at the end of forty-five minutes, using 5 mg. of dye per kilogram of body weight.

With these findings and this history, a diagnosis of Laennec's cirrhosis of the liver was justifiably made.

He was put on a high protein diet with a high carbohydrate intake, brewers' yeast, multiple vitamins, methionine and choline, liver extract, and diuretics. On three occasions abdominal paracentesis was performed in the hospital and large quantities of ascitic fluid removed. The icterus gradually decreased and the patient left the hospital in a somewhat improved condition after a few months' stay.

Following his discharge from the hospital the patient was followed in the outpatient department. He gets an abdominal paracentesis every two weeks. He gets mercurial injections and liver extract every two weeks.

His blood chemistry is not changed remarkably. His bromsulfalein retention is still 36 per cent at the end of forty-five minutes; his blood count stays about the same, and his icterus index is 16.

I asked about a cephalin-cholesterol, because of the evidence of liver damage, and I found that it was 4+ in twenty-four hours. While this is not a test for liver function, it does indicate liver damage and is a very helpful test. He states that he feels good now but that he is not able to work. He rests a good deal and stays in bed much of the time. He has no evidence of neuritis. He is not using alcohol and has not used it for the past six months. Interestingly enough, after he gets the paracentesis and other medications, he states that he gets cramps in his legs. I questioned him about this specifically, as it is not uncommon for cramps in the legs to result from mercurial diuretics, particularly when there is a low sodium intake. Mercurial diuretics cause a sodium diuresis, which precedes the water diuresis. These patients lose so much sodium that they get essentially the same condition that is found in heat cramps: that is, they lose too much sodium. The cramps can be avoided by giving these patients sodium before giving the mercurials, if these cramps are of any considerable severity after use of mercurials.

X-ray examinations usually reveal a normal esophagus but may give evidence of esophageal varices.

LIVER FUNCTION TESTS

The liver function tests are usually of great value in making a diagnosis of cirrhosis of the liver. A few of the many liver function tests may be selected for aid in early diagnosis. We talked about the icterus index, the prothrombin time, the cephalin-cholesterol flocculation test, and the bromsulfalein test. Incidentally, the bromsulfalein test is not of so much value when the patient has jaundice. An additional incidental liver function test is sometimes made when the patient is given a gallbladder dye series, and the result is a poorly functioning gallbladder. Sometimes this result is due to the liver being poorly-functioning rather than the gallbladder. It is important not to take out the gallbladder when the trouble is due to a poorly-functioning liver.

The serum albumin is another evidence of liver function and it is of considerable value prognostically for if these patients get better their serum albumin rises, and if they do not improve it usually declines.

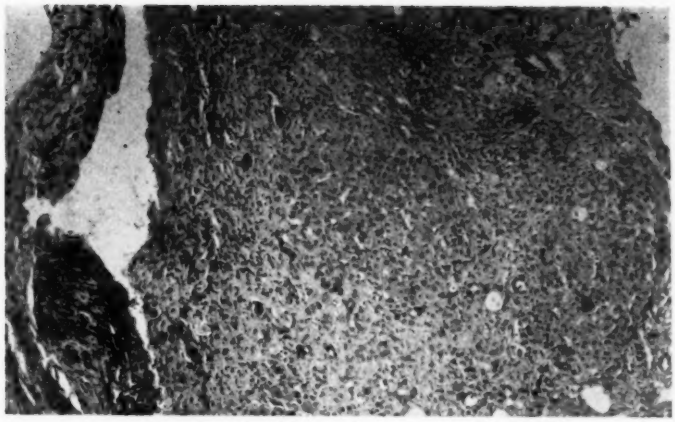

Figure 1. Needle biopsy showing a far-advanced cirrhosis of the liver.

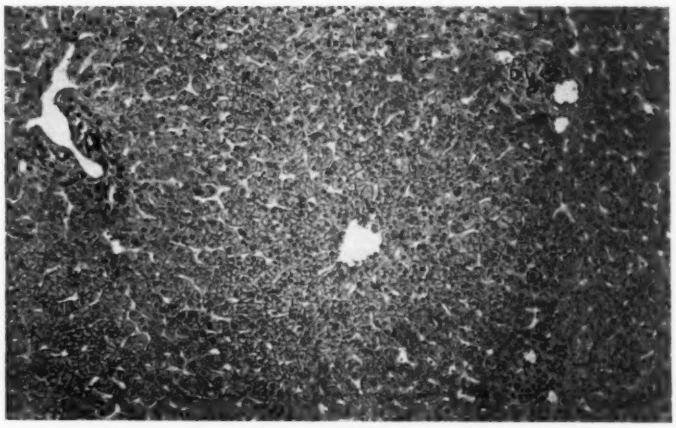

Figure 2. Normal liver showing a good central vein in the center.

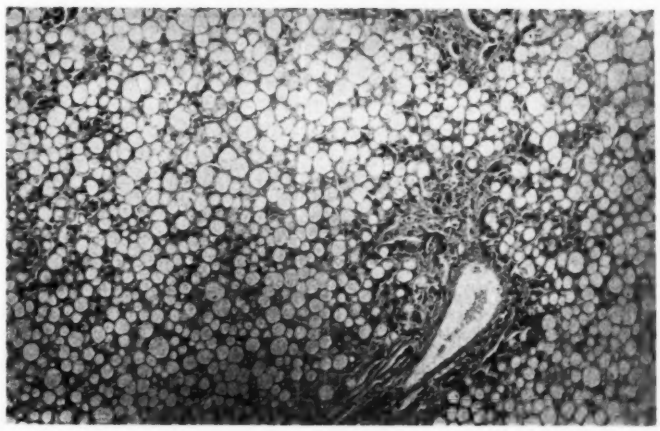

Figure 3. Marked fatty changes in the liver with a minimal amount of portal fibrosis.

One can, in the office, obtain ascitic fluid and estimate the specific gravity. If it is below 1.015 it is a transudate and that fits in with the diagnosis of cirrhosis of the liver. Incidentally, when you have the needle in the abdomen you can put in a couple of cc.'s of a mercurial diuretic and get a good diuresis. If the ascitic fluid is bloody, a malignancy is probably present if a bloody tap can be excluded. If one finds a specific gravity of over 1.015 an exudate is to be considered which may be due to some such thing as tuberculous peritonitis.

A liver biopsy may be necessary at times in order to make a diagnosis. There are three things you should have if you are going to do a liver biopsy. The patient should have an easily palpable liver, which extends well below the costal margin anteriorly. This man did not have such an easily palpable liver and, therefore, he is not a candidate for needle biopsy. The second factor in this patient which contraindicates a liver biopsy is his low prothrombin time. In the third place, all patients having needle biopsies should be hospitalized in case a surgical emergency should arise. The diagnosis in this case is so clear that a surgical biopsy is not indicated.

FIGURE 1 is a needle biopsy which shows a far-advanced cirrhosis of the liver.

A normal liver showing a good central vein in the center is seen in Figure 2. This vein collects all the blood which leaves the liver. The portal space, with the portal vein coming from the intestines, the bile duct, and the hepatic artery are all readily seen in this area.

Figure 3 reveals marked fatty changes in the liver with a minimal amount of portal fibrosis. This 53-year-old undernourished patient died from shock following urinary retention from a urethral stricture. A liver lesion such as this is reversible. These patients often die suddenly from liver failure.

Severe fatty changes with more definite diffuse fibrosis of the liver are shown in Figure 4. This 43-year-old chronic alcoholic patient died in cholemia with evidences of marked portal hypertension, including esophageal varices and some ascites. It should be emphasized that the fatty infiltration caused distention of the liver cells with fat and produced portal hypertension in spite of relatively little fibrosis. These cases respond best to therapy because the fatty lesions are reversible.

This 59-year-old patient (Figure 5), a Mexican "wino" who drank one pint of wine per meal as long as he could remember, had an adequate food intake so that there was very little fatty infiltration. He had many abdominal paracenteses for ascites. He finally died in a cholemic stupor. A lesion like this is plainly irreversible and is not amenable to dietary therapy.

The vigor with which a patient with cirrhosis of the liver will be treated depends upon (1) the certainty of the diagnosis, (2) the realization of the seriousness of the prognosis, and (3) the knowledge that the treatment is reasonably effective.

The seriousness of the prognosis is indicated by the work of Ratnoff and Patek. These and other co-workers compared the results of their old treatment of cirrhosis of the liver with newer methods of therapy which they have been influential in promulgating. Using the onset of ascites alone as the evidence for liver decompensation in 120 cases they found that instead of the older mortality of 61 per cent in the first year only 35 per cent died in that same period. At the end of two years 50 per cent were dead after the newer therapy compared with a 79 per cent mortality in the older series. At the end of five years 70 per cent of the cases had died following the newer therapy compared with 93 per cent in the old series.

DIET

The most important difference between the older methods of therapy and the new therapy is dietary. The real change in the diet is from a low protein to a relatively high protein diet. When I finished a residency in medicine, more than fifteen years ago, there was one thing we were sure of, and that was that a low protein diet was needed in the treatment of cirrhosis of the liver. Now we are certain, because of abundant clinical and good experimental evidence, that a rather high protein diet is most helpful. Milk, eggs, meat, cottage cheese, and other foods high in protein should be appetizingly provided.

The art of getting the patient to eat must be exploited to the fullest extent. If the patient cannot eat food he can often drink food. Skimmed milk is the best basic food in this disease. It is also a good vehicle and in it one can put eggs, skimmed milk powder, and such protein supplements as Casec. Your dietitian will help you with this program and see that a good protein diet is provided

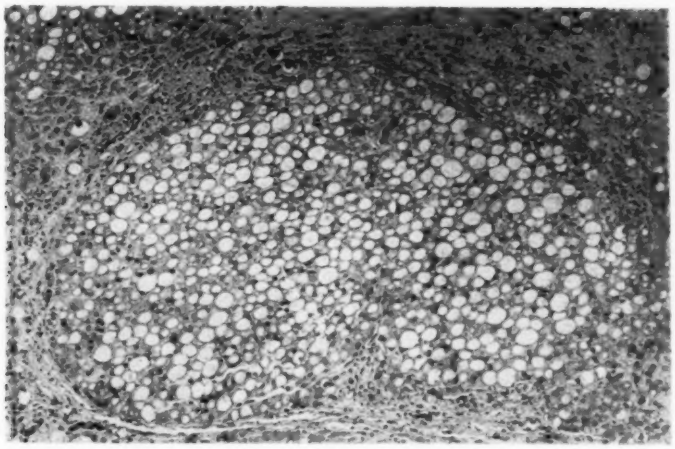

Figure 4. Severe fatty changes with more definite diffuse fibrosis of the liver.

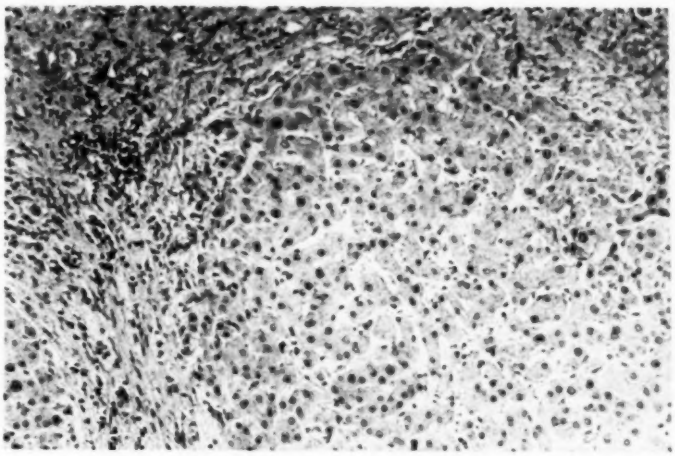

Figure 5. Little fatty infiltration. Lesion is plainly irreversible and not amenable to dietary therapy. Many abdominal paracenteses for ascites.

which can be swallowed, in liquid form if necessary. Water can be interdicted until the food intake is adequate.

In the ordinary diet with adequate protein intake there is enough methionine and choline to accomplish the preventive and therapeutic purposes in this disease. Until the protein intake is very adequate choline or methionine should be given. One can get a good-tasting syrup of choline dihydrogen citrate and it can be given with advantage in doses of 1 or 2 teaspoonsful three times a day.

Alcohol should be interdicted, although the evidence is not good that alcohol itself is the direct cause of cirrhosis of the liver. It may be a noxious agent, but we do not know that. If these people keep up their alcohol intake their chances are very poor that they will eat properly.

The common accompaniment of multiple neuritis in this disease suggests that a routine use of multiple vitamins is in order. One can give 3 to 5 cc. of crude liver extract (2 units per cc.) three times a week. Larger doses by intravenous means,

with a special preparation, may be indicated if the appetite is very poor. Mercurials are given just as they are in heart disease to relieve edema and ascites. If they work they should be used intramuscularly or intravenously in whatever frequency proves to be effective. Paracentesis should be accomplished as often as is necessary if mercurials fail to control the ascites, as this procedure reduces portal hypertension and makes the patient more comfortable.

Antibiotics are responsible for some of our improved statistics. About one-third of these cirrhotics die from cholemia, about 25 per cent from hematemesis, and most of the rest of them die from infections or intercurrent diseases. Penicillin often controls infections and prolongs the life of these patients.

The sulfonamide drugs may help in intercurrent infections and are not contraindicated by the liver damage.

Rest should be judiciously employed. These patients are willing to rest at first, and generally one can let them follow their own dictates.

If a patient develops cholemia, intravenous glucose with 300 mg. of niacinamide and 100 mg. of vitamin B will sometimes bring them out of their stupor or coma. Vitamin K is to be used when there is bleeding and the prothrombin time is low.

Hematemesis is controlled symptomatically.

Surgical procedures, except for abdominal paracentesis and biopsies, are usually hazardous and not helpful.

In summary, cirrhosis of the liver is a serious chronic liver disease characterized by fatty infiltration and a progressive fibrosis. The cause is unknown, but important factors in its development are chronic dietary deficiencies, particularly deficiencies in the proteins. The common precipitating factor of this protein deficiency, in this country, is alcoholism.

The control of this disease is essentially the prevention of chronic alcoholism and malnutrition and the over-correction of the dietary deficiencies once the disease is discovered.

CANCER PROGRESS CITED BY INSURANCE STUDY

Recent progress in cancer control is cited in the *Statistical Bulletin* of the Metropolitan Life Insurance Company, which publishes data to show that in the past decade the age-adjusted death rate from cancer among insured white females, ages 1 to 74, has declined 11 per cent. Within the age range from 25 to 74 years, where the cancer toll advances sharply with age, each period of life showed a reduction, and at ages 55 to 64, the drop was 15 per cent.

Among white men, the mortality from cancer remained relatively stable in the past decade, in contrast with the marked upward trend in evidence for many years prior to that time, the report states. The comparisons are made between the 1936-38 policyholder death rates and the 1946-48 rates.

SCIENTISTS EXPRESS CONCERN WITH RESEARCH PROBLEMS

The dilemma of the modern scientist in facing problems which are a challenge both to his research work and his views on world problems is expressed by eleven noted scientists who are contributors to a new edition of the book, *Science in Progress,* published by the Yale University Press. The volume is edited by George A. Baitsell, biology professor at Yale. Professor Henry D. Smyth of Princeton University, author of an historical article, "From X-Rays to Nuclear Fission," concludes that the scientific method has led to remarkable discoveries in the laboratory but that "mankind has failed to understand the lesson of method." He states: "The thoughtful scientist reviewing his present situation is deeply concerned. The world . . . seizes on the power released by science and with an eager impulse toward suicide turns it to purposes of destruction."

Contributors of articles on medical research are Dr. Wendell M. Stanley and Dr. Rene J. Dubos, both of Rockefeller Institute. Dr. Stanley points out that despite new discoveries on viruses, little is known about their biological and chemical nature.

DIAGNOSTIC CLINIC

The Surgical Treatment of Hypertension

WINCHELL McK. CRAIG*

MAYO CLINIC, ROCHESTER, MINNESOTA

PHYSICIANS are continually being asked how to select suitable patients in the surgical treatment of hypertension and at what stages in the development of hypertension an operation on the sympathetic nervous system should be performed. In the diagnosis and evaluation of hypertension it is important to take into consideration a number of fundamental factors. In the first place, it must be kept in mind that the blood pressure is maintained by three physiologic factors; namely, the viscosity of the blood, the pumping power of the heart, and the size and caliber of the blood vessels. In the hypertensive patient it has been shown that the viscosity of the blood remains unchanged and the force of the heart remains normal; the only physiologic change which can be proved consists of narrowing of the lumen of the blood vessels.

It is also necessary to remember another factor which Ayman[1] pointed out years ago; namely, the hereditary influence in all cases of essential hypertension. He showed by investigation among his patients that hypertension developed in only 3 per cent of those whose parents had no history of high blood pressure. When one parent suffered from hypertension, the incidence among the children was 28 per cent and if both parents were suffering from hypertension, the incidence was 45 per cent. This emphasizes the genetic factor in essential hypertension.

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Presented November 9, 1948, before the meeting of the Interstate Postgraduate Medical Association of North America, Cleveland, Ohio.

It has also been found that in patients with hypertension of unknown origin further investigation is necessary with regard to the glands of internal secretion; particular attention must be paid to the adrenals because some patients with elevated blood pressure may have a pheochromocytoma or tumor of these glands. Urologists have shown very definitely that there can be a coexisting lesion of the kidney in connection with hypertension. The removal of the damaged kidney brings the blood pressure down. In thinking of the surgical treatment of hypertension, then, the neurosurgeon has to be sure that he is dealing with essential hypertension, and any known cause or factor must be excluded before he considers the surgical treatment of hypertension by operations upon the sympathetic nervous system.

In reviewing the series of patients with hypertension who have undergone operation at the Mayo Clinic, I have been very much impressed with several factors. The treatment of essential hypertension should probably consist of three different phases; namely, expectant, physiologic, and palliative. The expectant treatment should be instituted early in the development of the disease, especially if there is a known hereditary background. The physiologic treatment should be divided into two parts, the medical and the surgical. The palliative treatment is the treatment of hypertensive persons whose disease has progressed to advanced stages and has shown some irreversible changes.

It is well known that one cannot carry an increased blood pressure for a long time without having some changes in the kidney, thyroid, heart,

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brain, and peripheral circulation. Attention has been called to the fact that treatment of hypertension is still not very effective and many phases still remain unexplored. Medical treatment based on diet and different types of drugs should be carried out, and only after a thorough trial of medical treatment should surgical intervention be considered. If, while the patient is under observation and medical treatment, the blood pressure continues to remain high or progresses in severity, then surgical treatment consisting of operations upon the sympathetic nervous system offers such a patient the only opportunity for relief from symptoms and for reduction in blood pressure; in this connection it is preferable to speak in terms of control of the progress of the disease rather than in terms of cure.

In the diagnosis and treatment of hypertension, Wagener and Keith[2] have divided patients with hypertension into four groups. These groupings are really arbitrary and are based upon the severity of the disease, the appearance of the fundi, and the progress of the disease. Figure 1 illustrates how life expectancy over a period of seven years varies with the group into which the hypertensive patient falls. It is apparent that over a period of five years group 1 hypertension carries a mortality rate of 25 per cent, group 2 a rate of 45 per cent, group 3 a rate of 80 per cent, and group 4 a rate of 98 per cent. If these rates are accepted as a yardstick by which surgical results and any alterations in the course of the patient suffering from hypertension of any of the groups are measured, then it is possible to determine the effectiveness of surgical treatment.

Several factors with regard to this grouping of patients with hypertension are important. One is that hypertension which starts out as group 1 may progress to group 2, 3, or 4 over a short period of time. In the group 1 cases in which there is a fairly low mortality over a five-year period, one cannot expect to change the picture a great deal, and the question has been brought up as to whether or not surgical treatment is necessary in this group. My colleagues and I have assumed that a patient who is suffering from group 1 hypertension should be kept under observation and if the grouping or the severity of the disease increases rapidly over a short period of time, we have found that operation is definitely indicated to control the progress of the disease.

On the basis of the work of Ayman and his concept of hereditary influence as a background for essential hypertension, Hines and Brown[3] examined a group of school children and found that 10 per cent reacted positively to the Hines and Brown test; that is, that 10 per cent of the school children are the so-called hyperreactors and are possible candidates for the development of essential hypertension. This test consists of immersing the hands and wrists in ice-cold water and taking the blood pressure at definite intervals: if the blood pressure remains fairly stable, these patients are not hyperreactive. If, on the other hand, there is a definite increase in blood pressure, they should be labeled as hyperreactors.

Hines and Brown went even further and traced families in which there was a hereditary tendency toward the development of hypertension. They found that in families that intermarry and in which there is a predominance of hyperreactors, the children are more likely to have essential hypertension than are the children in families which do not have such a background. They followed a family in which it was known that a hypertensive

tendency existed on both sides. In 1932, 3 hyperreactors and 3 definitely hypertensive persons were found in this family. Eight years later, or in 1940, 2 members of the family were dead and the hyperreactors had hypertension. I bring this to your attention to illustrate the influence of heredity upon the development of hypertension in families.

This, of course, brings up the question of expectant treatment in families who have a potential or latent hypertensive tendency. In conjunction with dietary treatment, certain drugs are being used for the control of hypertension. Potassium thiocyanate is being used with some success in certain cases. Rutin has been administered to control vascular fragility. Veratrum viride and permutit Z, which is a combination of chemicals that bind the sodium in the diet but also bind calcium and electrolytes, are being administered. It has been proved in the physiology laboratories at the clinic that smoking of cigarettes produces a definite vasoconstriction; therefore, we feel that the smoking of cigarettes should be advised against for all patients suffering from hypertension.

The surgical treatment of hypertension should be reserved for those patients who do not respond to dietary treatment, to treatment with drugs, or to abstinence from smoking. From the historical viewpoint of the surgical treatment of hypertension, the first approach consisted of rhizotomy and splanchnic resections, with the removal of the lumbar sympathetic ganglia 1 and 2 below the diaphragm and the removal of the thoracic sympathetic ganglia 10, 11, and 12 above the diaphragm. These two operations were carried on simultaneously (Figure 2) and were called the supradiaphragmatic and the infradiaphragmatic operations respectively. In the diagram the hatch marks indicate the areas of anhidrosis or the lack of sweating which follows removal of the sympathetic ganglia.

Roth and I[4] have found that 14 per cent of the patients who undergo infradiaphragmatic sympathectomy at the clinic have anhidrosis up to and including the hip, 41 per cent have anhidrosis only up to the hip, 40 per cent have anhidrosis only up to the knee, and 4.8 have anhidrosis only below the ankle. When the infradiaphragmatic and the supradiaphragmatic operations were combined into an extensive thoracolumbar sympathectomy and splanchnic nerve resection, it was found that 27 per cent of the patients had postoperative anhidrosis up to the costal margin, 6.2 per cent only up to the hip, 20 per cent only up to the upper part of the thigh, 30 per cent only up to and including the knee, 12.4 per cent only up to the knee, and 4.2 per cent only in the foot (Figure 3).

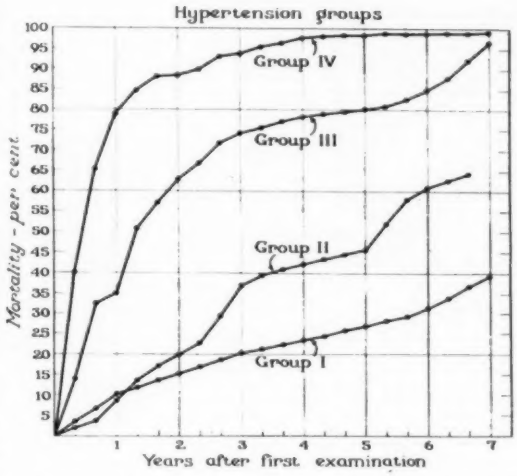

Figure 1. Relation between hypertension group and life expectancy.

THE results of the postoperative sweating test which all surgical patients undergo are rather interesting in view of the fact that the same operation was done on every patient. The results obtained bring up the question as to whether there is regeneration of the sympathetic nervous system or whether the anomalies in the sympathetic ganglia and rami are such that complete denervation is not always possible. This in no way reflects on the skill of the surgeon but brings out a fact which our anatomic atlases have neglected to show us; namely, that contrary to the location of the central nervous system which is usually found in its normal place, the sympathetic nervous system may send anomalous rami by devious pathways to the lower extremity.

In attempting to prove whether or not regeneration actually takes place, a patient was examined eight days after operation and two years after operation, and it was found that there was no evidence of regeneration of the lumbar sympathetic trunk. In spite of this evidence of lack of regeneration there are cases on record in which the patient

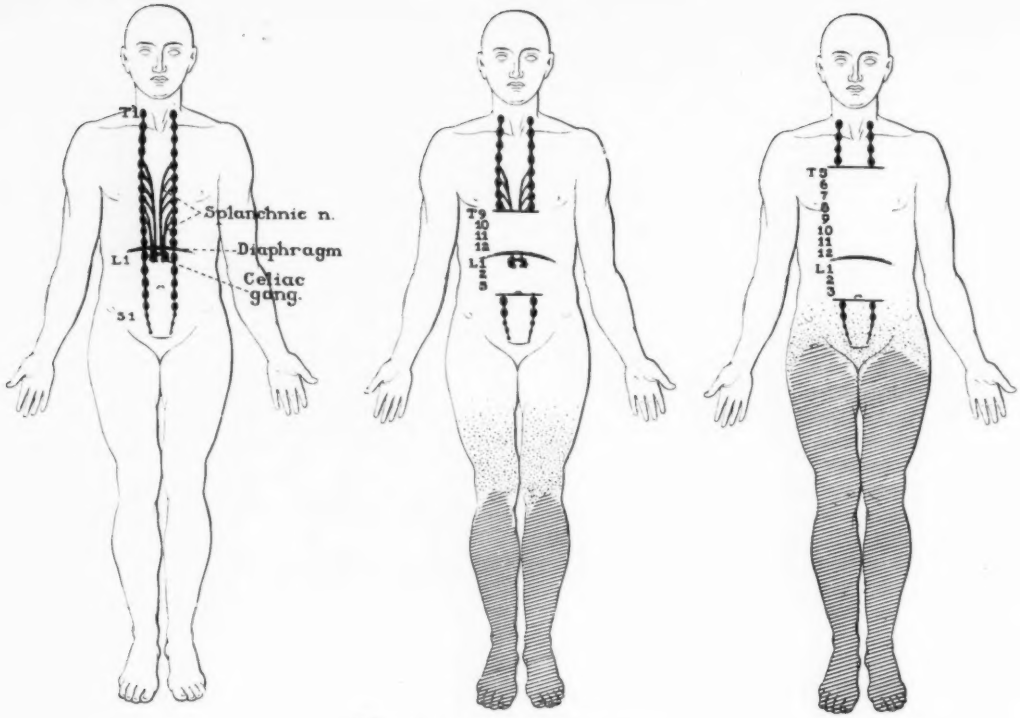

Figure 2 *(Legend on opposite page.)*

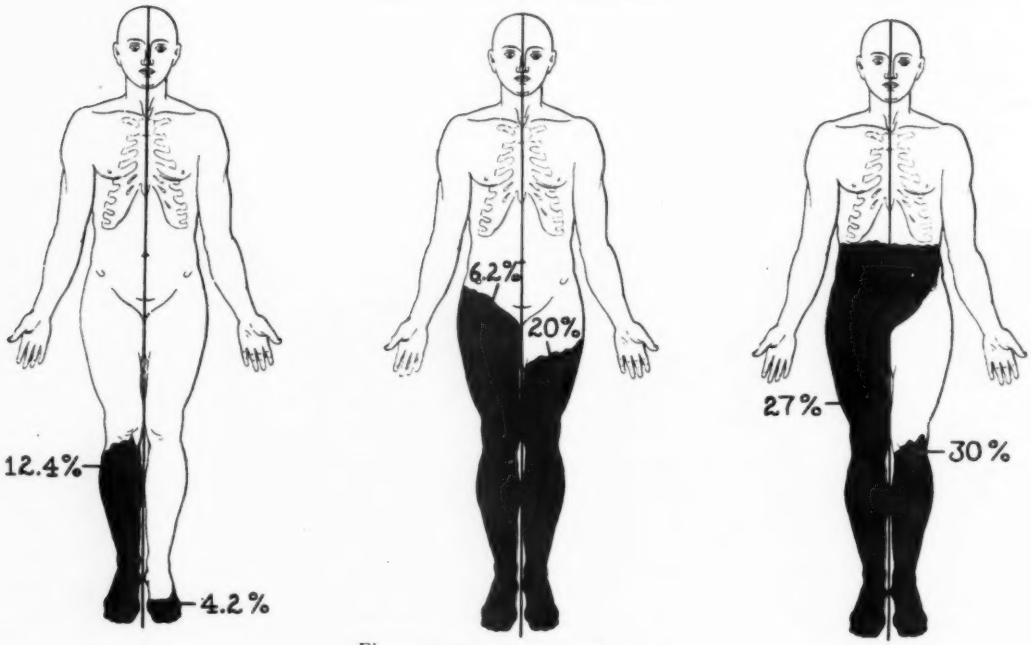

Figure 3 *(Legend on opposite page.)*

was operated upon a second time and definite evidence of regeneration was found.

CASE REPORTS

DATA on a few patients to illustrate some of the points which I have attempted to demonstrate will be presented.

Case 1—The first case (Figure 4) is that of a man 40 years of age who in 1944 was found to have hypertension and was turned down for life insurance. His blood pressure registered 190 systolic and 110 diastolic, expressed in millimeters of mercury. A year later he had hypertension, group 1, as evidenced by the severity of the disease and the appearance of his optic fundi. One year later his hypertension had increased in severity and he was found to have a group 3 hypertension. A thoracolumbar sympathetic ganglionectomy and splanchnic nerve resection was done. His immediate postoperative blood pressure approximated normal. He was examined in 1947 and again in 1948, two years after the operation, when he was found to have normal fundi and normal blood pressure. It has been interesting to note that he has been very careful of his weight, has watched his diet, has not smoked since his operation, and has taken excellent care of himself. Even though he is in rather strenuous work, his blood pressure remains normal.

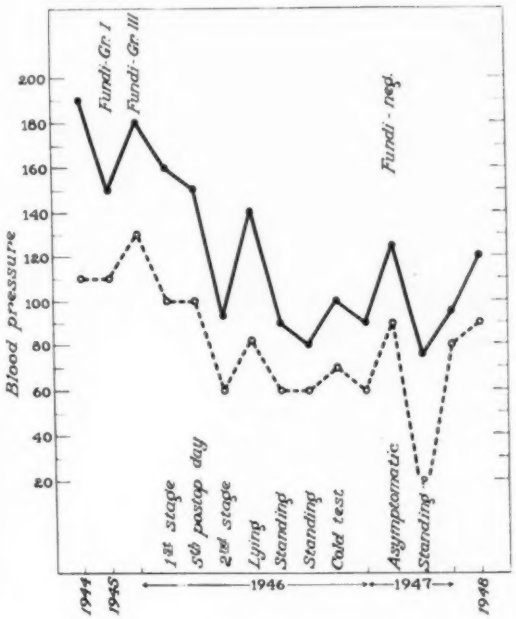

Figure 4. Chart of a patient with sudden rise in grouping of hypertension and return from group 3 to normal following operation.

My colleagues and I have probably learned more with regard to the postoperative effect of sympathectomy in the treatment of hypertension from our physician patients, who have been most cooperative in informing us of the changes in blood pressure as well as of the subjective relief which they have obtained.

Case 2—A physician 41 years of age (Figure 5) has been under our observation for a number of years. In 1935 his blood pressure was 135 systolic and 90 diastolic. In 1938 his blood pressure returned to normal levels, being 120 systolic and 90 diastolic. In 1940 he maintained the same level. He was seen again in 1942 and 1943, and in 1945 because of a definite elevation of blood pressure and a development of group 1 plus hypertension. He was placed on potassium thiocyanate treatment. This treatment controlled the progress of the disease, but in spite of this the blood pressure increased and the subjective symptoms became more severe. For that reason, in 1946 an extensive thoracolumbar sympathectomy and splanchnic resection was done. Two years later his fundi were normal and his blood pressure was maintained at approximately 135 systolic and 90 diastolic, exactly where it was in 1935, thirteen years previously. This physician is carrying on with his normal practice. He finds, however, that he is much more comfortable if he does not indulge in strenuous exercise, and he has given up golf because he feels much better without it.

In this particular case, I do not feel that the hypertension has been cured but I think that by bringing the patient's hypertension from a group 1 plus down to a normal level we have controlled the progress of his disease.

Not all patients have such a satisfactory result as the foregoing one.

Case 3—A man 32 years of age was found to be suffering from hypertension with a pressure of 230 systolic and 135 diastolic in 1934. He had very few symptoms. He was treated with potassium thiocyanate but his blood pressure dropped very little. In 1946 he began to have symptoms and was found to be suffering from group 3 hypertension. With the patient under the effects of sodium amytal (amo-

Figure 2. Diagrammatic representation of the intact sympathetic nervous system and of the different types of operation, with resulting anhidrosis as indicated by the shaded areas.

Figure 3. Anhidrosis following sympathectomy. Variation in the extent of denervation is indicated.

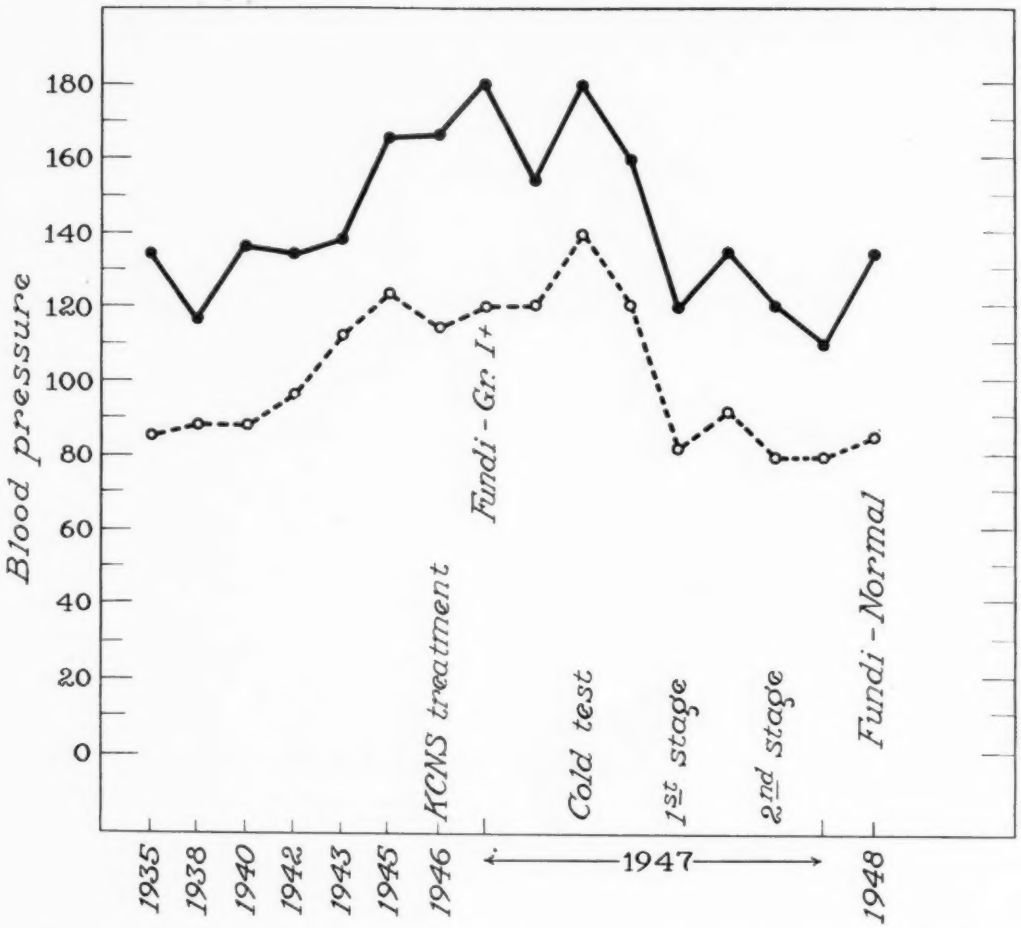

Figure 5. Chart of a patient showing a rise in blood pressure over a period of time in spite of medical treatment and return to normal following operation.

barbital sodium) his blood pressure dropped to 150 systolic and 120 diastolic.

Extensive thoracolumbar sympathectomy and splanchnic nerve resection was carried out. He was completely relieved of his symptoms although his blood pressure was not lowered materially; because of circumstances at home, he left the hospital before postoperative sweating tests could be made. When he returned in November 1946 for examination, the sweating test disclosed that he had anhidrosis only to the midthigh on the left. This indicated that he probably had an abnormal distribution of the sympathetic ganglia on the right, and he was advised that another operation should be done in order to examine the sympathetic nerve supply to his right lower extremity. He had obtained such a satisfactory subjective result, having been relieved of his headaches, that he asked to put off the operation for an indefinite period in view of the fact that he was involved in a very serious business transaction. Before he could return for operation, however, he had a coronary occlusion.

THIS case demonstrates the necessity of postoperative sweating tests, for in spite of extreme care taken in operating upon the sympathetic nervous system, the anatomic distribution of the rami sometimes prevents obtaining denervation of the lower extremity as manifested by anhidrosis.

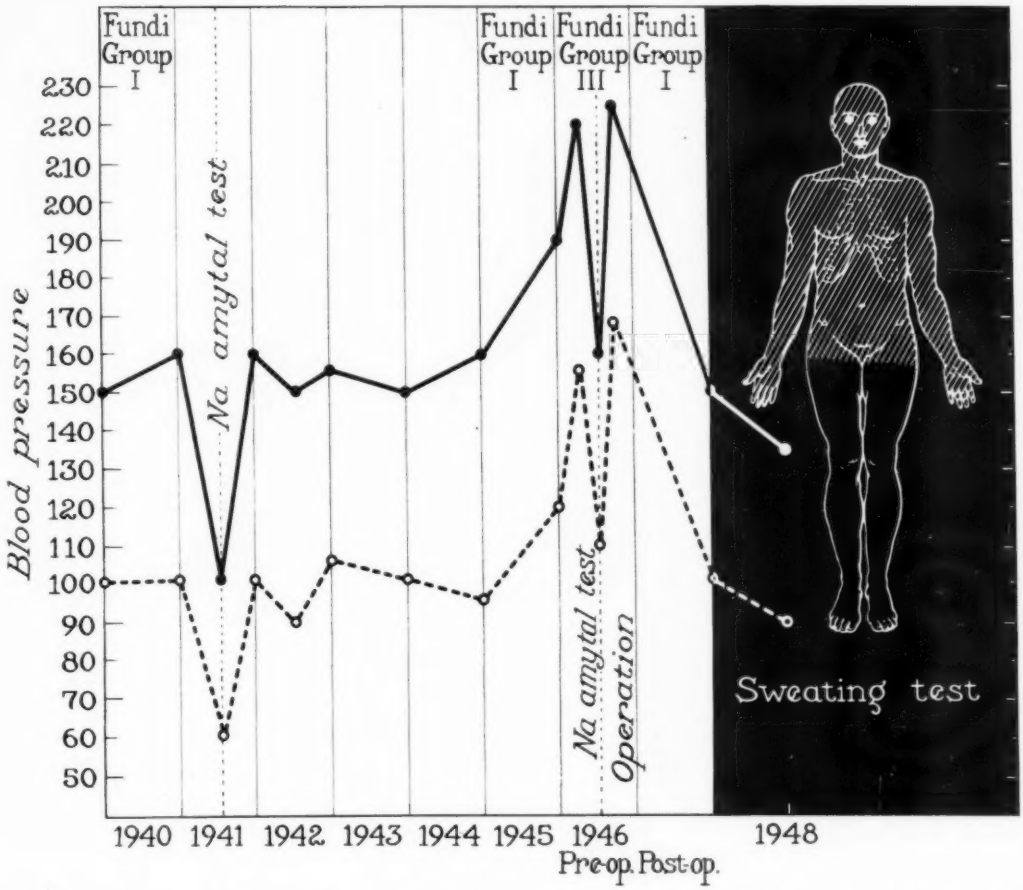

Figure 6. Chart of a patient showing blood pressure readings over a period of eight years, with a sudden increase in severity of hypertension from group 1 to group 3. Following operation reduction in blood pressure and fundi continued to be characteristic of group 1. There was anhidrosis below the upper portion of both thighs.

Case 4—Another physician 34 years of age at the time of operation had been under observation for six years (Figure 6). In 1940 he had hypertension, group 1, with blood pressure averaging 150 systolic and 100 diastolic. His blood pressure and the appearance of his fundi remained unchanged. In 1941 he had a sodium amytal test, as a result of which his blood pressure dropped to 100 systolic and 60 diastolic, showing he still had a flexible vascular system.

The blood pressure remained unchanged, with very few symptoms and in the same grouping until 1945, when, between the middle of 1945 and 1946, the grouping changed suddenly from a 1 to a 3 and he began to suffer from headache and fatigue. At this time the sodium amytal test was done, and the blood pressure was reduced to 160 systolic and 110 diastolic. Operation was carried out at this point, and two years later his blood pressure remained at an average of 130 systolic and 90 diastolic; his fundi were still characteristic of group 1 hypertension, evidencing some irreversible changes in the blood vessels. The sweating test revealed definite anhidrosis below the upper portion of both thighs. This physician also is carrying on with his usual duties, completely relieved of his symptoms.

AGAIN I do not call this a cure but rather, control of the progress of his disease.

My colleagues and I have been impressed, in reviewing our series of cases, that the patients with

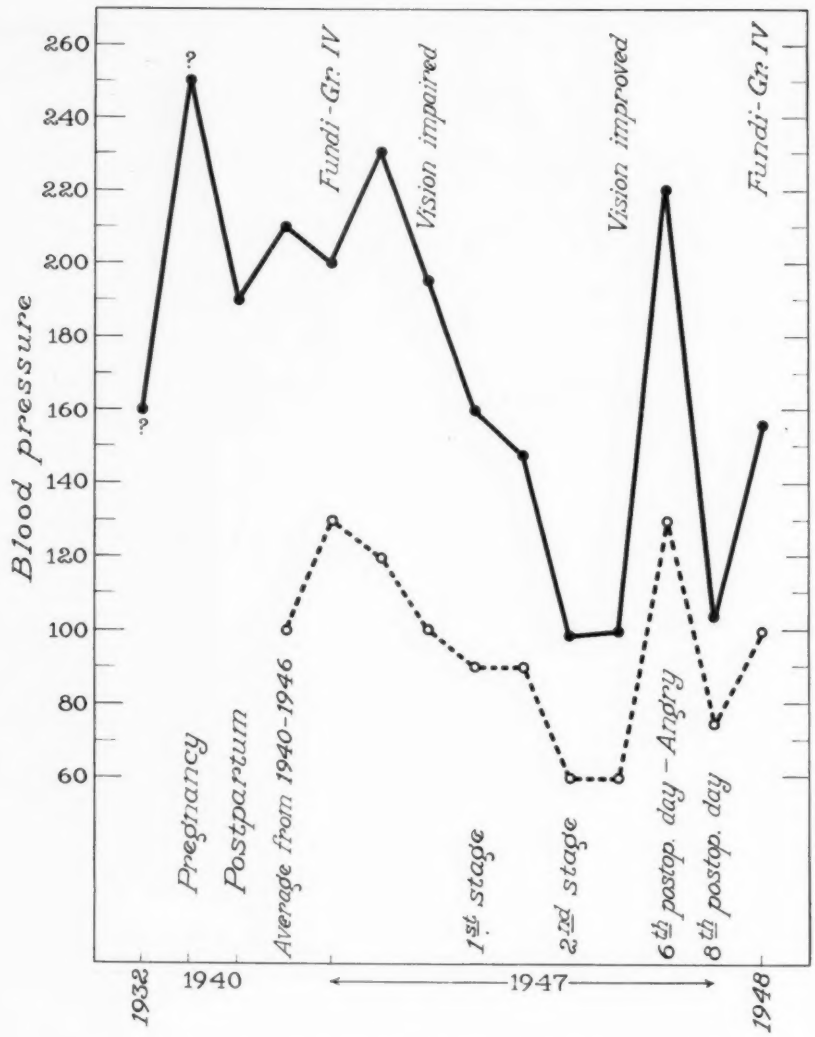

Figure 7. Chart of a patient showing blood pressure readings over a period of years with development of group 4 hypertension and with visual impairment. Following operation, the grouping remained unchanged although vision improved and subjective symptoms were relieved.

advanced disease, that is, those of group 4, whose hypertensive changes have been in evidence for a long time, do not do as well after operation as do those of groups 2 and 3. It is in group 4 that we believe that the operation is palliative, as is demonstrated in the following case.

Case 5—A woman 44 years of age was a sister of a physician (Figure 7). Her brother knew that in 1932 her blood pressure was elevated, and during her pregnancy in 1940 we know that the systolic pressure was about 215. The average blood pressure from 1940 to 1946 was in the neighborhood of 230 systolic and 130 diastolic.

In spite of medical treatment her blood pressure remained high, her vision became impaired early in 1947, and

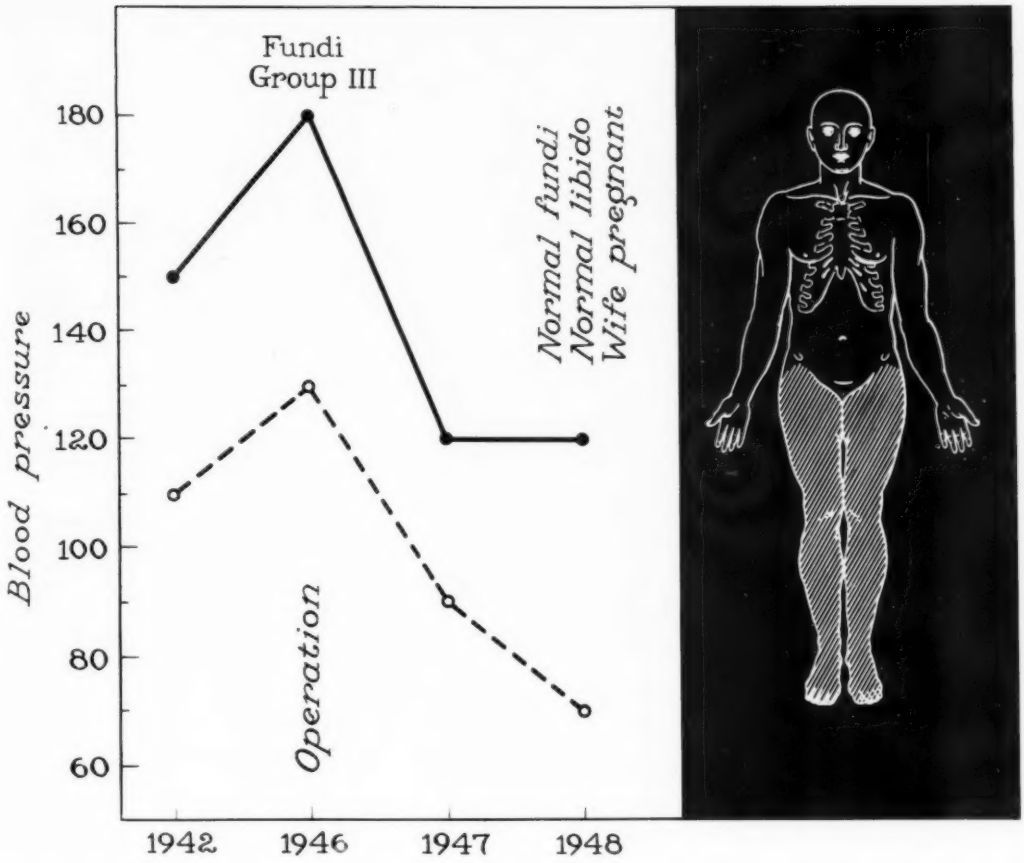

Figure 8. Blood pressure readings over a period of years in a case of group 3 hypertension. Two years after operation the patient was at work, relieved of subjective symptoms with normal fundi, normal libido, and wife pregnant.

severe headaches began. At that time operation was carried out as a palliative measure to relieve her headaches as well as to improve her vision. Her immediate postoperative reaction to the operation was very good, but it is significant that on the sixth postoperative day she became very much incensed over a small incident that happened in her room, and her blood pressure taken at that time registered 220 systolic and 130 diastolic.

Almost two years later her blood pressure ranged around 160 systolic and 100 diastolic. The fundi were still characteristic of group 4, and it was felt that she was actually suffering from group 4 hypertension; however, her vision improved and she was relieved of her headaches. The fact that she remained in group 4 for almost two years seems to mean that irreversible changes do take place after hypertension has been present for a long time.

In advising patients to have the operation for the control of their hypertension, we always hope to come across what we consider the perfect case. The following case illustrates what can be done when operations are instituted early in the development of the disease in fairly young people. This case also illustrates some of the problems which are encountered in discussing the operation with patients. It is a well-known fact that certain portions of the sympathetic nervous system cannot be removed without untoward effects. For instance, it is known that if the lumbar sympathetic ganglia are removed in the male, there is some interfer-

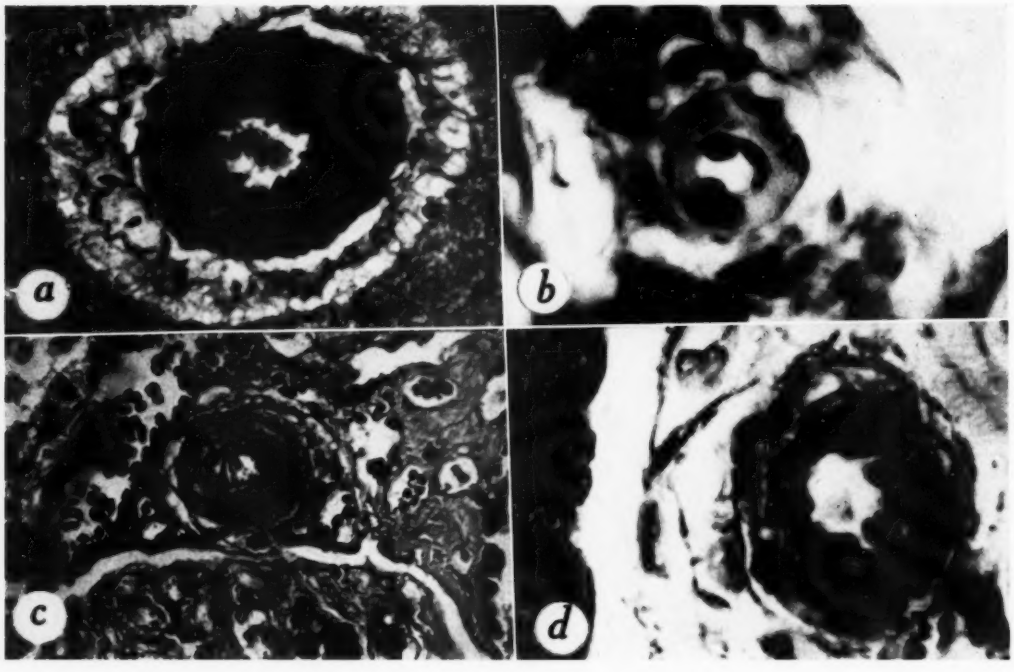

Figure 9. Arterioles from various organs of persons who had essential hypertension. *a.* Brain. *b.* Thyroid gland. *c.* Kidney. *d.* Myocardium (hypertension, group 4). (Reprinted with permission from FARBER, E. M., HINES, E. A., JR., MONTGOMERY, HAMILTON, and CRAIG, W. McK.: The arterioles of the skin in essential hypertension. J. Invest. Dermat. 9:285-298 (December) 1947.

ence with the libido and with the ability to have children.

Case 6—A male 29 years of age discovered he was suffering from mild hypertension in 1942 (Figure 8). In 1946 he became aware of increasing severity of symptoms and when examined was found to be suffering from group 3 hypertension. He underwent an extensive thoracolumbar sympathetic ganglionectomy and splanchnic resection. The immediate postoperative results were excellent; he was relieved of his headaches and other subjective symptoms and his blood pressure returned to the normal level of 120 systolic and 70 diastolic. Two years after the operation anhidrosis was present from the hips down, the fundi were normal, he said that he had normal libido, and he was very much delighted in stating that his wife was pregnant.

I feel that this is the ideal case—a man of 29 years who was suffering from group 3 hypertension which was not responding to medical management but who, two years after operation, had a normal blood pressure and was living a normal life. Patients who are considering the operation frequently ask about the percentage of men whose libido is affected. Poppen[5] in his series of thoracolumbar sympathectomies has found that 41 per cent of the men retain their libido and their sexual potency.

ONE of the reasons why neurosurgeons cannot expect materially to change the vascular tree by removing sections of the sympathetic nervous system is the fact that after a long time certain irreversible changes in the circulation take place throughout the entire body (Figure 9). Microscopic sections of the vessels in the different organs reveal, in the arteries, marked sclerotic changes which have become irreversible and cannot be influenced by diet, drugs, or operations.

Thus in any discussion of operations for the relief of hypertension, it must be kept in mind that sympathectomy is a physiologic operation in which no diseased tissue is removed. The object

of the operation is to increase the caliber of the blood vessels in the denervated part which in turn relieves the head of pressure within the vascular tree.

Farber and co-workers[6] at the clinic have shown very definitely that the extent of sclerosis of the blood vessels or the arterioles in the skin approximates that of disseminated arteriosclerosis which accompanies essential hypertension. In the light of these findings, then, it is evident that after hypertension has advanced to extreme degrees and caused irreversible changes in the vascular tree of the entire body, sympathectomy can produce only palliative results.

Before surgical treatment is started, every patient who is suffering from hypertension should be carefully studied and an effort should be made to distinguish between primary and secondary hypertension. If the hypertension is secondary, then the underlying cause should be isolated and treated. Those patients who fall into the category of primary hypertension should be treated conservatively, as many patients suffering from hypertension respond satisfactorily to dietary and drug treatment. If in spite of conservative treatment the hypertension persists and continues to progress in severity, surgical treatment should be instituted.

SUMMARY

With regard to the surgical treatment of hypertension, essential hypertension of obscure cause should be looked upon as a progressive, serious disease requiring careful observation and treatment. The treatment should be instituted in the early stages and probably should be classified as expectant, physiologic, or palliative.

The expectant treatment should consist of determining whether the patient is a hyperreactor and has early hypertension, of instruction as to the harmful effect of nicotine and emotional stress and strain, and of education in the proper methods of living.

Physiologic treatment comprises both medical and surgical measures and is indicated in the early stages of the disease before irreversible changes have taken place in the vascular and organic tissues of the body. This type of therapy is instituted to arrest the progress of the disease.

The medical treatment consists of dietary and drug therapy. The surgical treatment consists of extensive thoracolumbar sympathectomy and splanchnic resection to relieve the vasomotor spasm of the vessels of the splanchnic region, abdomen, and lower extremities.

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HEART DISEASE DEATHS INCREASE AMONG INSURED

Reports of the Institute of Life Insurance indicate that, while deaths from all causes among ordinary life insurance policyholders dropped to a new low in 1948, the heart disease death rate rose in the same period to a record high and accounted for more than half the total. For this policyholder group last year, the total death rate was 625.1 per 100,000.

Deaths from the chief cardiovascular-renal diseases, including diseases of the heart, cerebral hemorrhage, and nephritis, were 327.9 per 100,000, constituting 52 per cent of the total. Cancer was second as a death cause, accounting for 98.7 per 100,000. The 1948 experience among industrial insurance policyholders followed a similar pattern but on a higher level, due to the difference in types of business; industrial policyholders are not generally subject to medical examination upon application for policies.

SCIENTIFIC EXHIBIT

Roentgenographic Studies of the Cervical Spine

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Because of its peculiar structure and function the upper spine is predisposed to sprains, partial dislocation, nerve root irritation, and degenerative changes. For a thorough examination of this region the following roentgenographic studies have been found desirable: 1. Lateral stereoscopic (dorsal extension). 2. Anterior flexion. 3. Chewing stereoscopic PA. 4. AP through the mouth. 5. Right and left 45° oblique, eight films in all.

The Anterior Curve

A lateral roentgenogram of the normal cervical spine at rest reveals the bodies arranged in a symmetrical anterior curve. Their posterior surfaces form the anterior wall of the spinal canal. (Figure 1.) In the absence of trauma the cervical spine maintains its anterior curve even in cases with advanced disk degeneration.

Upon anterior flexion of the normal neck, the curve is reversed but it always remains symmetrical at all points. In the cadaver specimen it is impossible even by counter pressure to produce angulation at one point, but if the posterior joint capsules are cut the curve may be replaced by forward angulation at that level.

Angulation

Following severe trauma to the neck, often of a "snap-the-whip" character, the normal anterior curve may become replaced by forward angulation of the cervical spine at one point. (Figures 2 and 3.) This would seem to indicate a partial bilateral subluxation of the injured posterior joints. Protective muscle spasm is usually present. Partial or even complete recovery of the normal anterior curve may occur with appropriate treatment. Lesser degrees of injury may show as a straightening of the anterior curve, but forward angulation indicates a more severe injury. If subluxation is recent, no bony bridging will have taken place, but calcification in the anterior longitudinal ligament may be noted later, bridging the intervertebral space in an attempt to stabilize this weakened level of the spine. The intervening disk may become thinned or complete fusion of the adjacent vertebral bodies may result with final absorption of the intervertebral disk. (Figures 4 and 5.)

Figure 1. Lateral view of cervical spine showing normal symmetrical anterior curve. Spot on arch of C2 represents posterior surfaces of spinal canal.

Figure 2. Post-traumatic forward angulation of the upper cervical spine above the level of the fourth disk.

Flexion—Extension Studies

Comparative lateral roentgenograms of the cervical spine made at the extremes of forward flexion and dorsal extension will show, in the forward position, the dorsal spinous processes widely separated, while upon dorsal extension they become closely approximated. (Figures 6 and 7.)

Injury and disease interfere with this movement between the various cervical segments so that either from spasm or fixation the flexion-extension studies may reveal a lack of movement between the various segments either at one level or involving the whole cervical spine. That is, two or more of the spinous processes do not separate when the head is bent forward. Upon subsequent examination it will be found in some cases that complete recovery of normal movement has taken place, in others the fixation seems to be permanent.

By this method it is possible to furnish roentgen evidence of injury and of progress in recovery even when the roentgenogram does not show other evidence of bone or joint injury. Surprisingly enough a considerable amplitude of movement may still persist in cases of advanced disk degeneration with disk thinning and even spur formation.

Gliding Movement

Examination of those cervical vertebral bodies below the second reveals the upper surface saddle shaped with the lateral margins raised above the level of the central portion. The undersurface of the body represents a section of a cylinder with its axis transverse.

The flexion-extension studies show not only a flexion between the bodies with separation of the spines, but also a gliding of each vertebral body backward and forward upon the one beneath it. Measurements indicate that the point of greatest amplitude of this gliding is about the mid-cervical region. This is the level of maximum disk degeneration noted later in life. It would seem to show that probably wear is a factor in producing such degenerative changes. In other words the intervertebral disks wear out. (Figures 6 and 7.)

Figure 3. Mrs. J. S., age 48. Forward angulation of cervical spine following automobile accident. Some chronic degeneration with thinning of fourth, fifth, and sixth disks.

Figure 4. Mrs. J. S. 12 years later. Complete fusion of fourth, fifth, and sixth disks with fusion of the fourth and fifth posterior articulations. The spine has become somewhat demineralized during this period and the patient has suffered severely from radicular pain referred to the shoulders and down the arms during this twelve-year interval.

PA Chewing Technic

The postero-anterior view, according to the method of Jacobs, is made with the patient lying prone, forehead resting on a sand bag, and the head immobilized by a fixation band. The tube target is directly over the occiput. The patient moves the jaw rapidly while holding the head absolutely still for a relatively long exposure of six to eight seconds. Such a postero-anterior roentgenogram will show: the alignment of the spinous processes, the thickness of the disks, the posterior articulations and the pedicles with their interpedunculate distance representing the size of the foramina. Constricted foramina exhibit a decrease of this measurement between pedicles. (Figure 8.)

The 45-Degree Oblique Cervical Technic

In the lumbar and dorsal regions the intervertebral foramina open from the lateral walls of the spinal canal. In the cervical region, however, they are directed laterally and forward about 45° to the sagittal plane and slightly downward.

The roentgenogram is best made with the patient sitting upright, spine erect, chin up, the occlusal plane of the teeth horizontal, and the shoulder of the side to be visualized against the vertical plate holder. The latter should be at such a height that the upper end of an 8 by 10 inch Lysholm grid cassette is on a level with the patient's ear. Use a measuring triangle of thin wood with angles of 45°, 90°, and 45° about 18 inches long on each of the two short sides. By sighting across the triangle downward from above the patient, arrange the transverse plane of the shoulders and the sagittal plane of the skull each 45° to the plane of the film. The head may be steadied by a small block between the cheek and the plate holder. The target of the tube is 6 feet back of the patient and the central ray is directed downward 10° and toward the mid-cervical region.

Figure 5. Mrs. J. S. taken five years after Figure 3. Forty-five degree oblique study showing normal foramina at C2 and C7. Foramina 5 and 6 encroached by exostoses projected backward from the intervertebral disks. Foramen number 3 encroached upon by arthritic exostoses projecting forward from the posterior articulation. Left-hand arrows indicate poorly visualized pedicles; right-hand arrows indicate widened space between the fourth and fifth neural arches caused by the angulation.

Figure 6. Anterior flexion. Spinous processes widely separated. Black lines indicate posterior surfaces of vertebral bodies, the lower posterior corner of each vertebra being anterior to the upper corner of the vertebra below it.

Figure 7. Posterior flexion. Spinous processes closely approximated. Lower posterior corner of each vertebra now posterior to the upper corner of the vertebra below it. This indicates a gliding of the vertebral bodies backward and forward upon each other.

Figure 8. PA chewing film showing intervertebral disks and pedicles. Large exostoses project from the left side of the fifth and sixth disks. These encroach upon the intervertebral foramina. See Figure 9.

This technic visualizes all of the cervical foramina of the side next the film beginning with the foramina beneath the second vertebra. There is, of course, no intervertebral foramen directly beneath the first segment.

The oblique roentgenogram may also be made with the patient lying on the Bucky table, the sagittal plane of the skull and the plane between the tips of the shoulders at a 45° angle to the table top. The central ray passes vertically from behind and through the atlanto-occipital joint. The patient is well supported by sand bags and may be asked to move the jaw while the exposure is being made.

The Normal Oblique Cervical Roentgenogram

A roentgenogram of the cervical spine made according to the foregoing technic reveals the intervertebral foramina in their normal shape and position. The topmost or second cervical is oval and those below this point are shaped, as Schmorl has described, somewhat like the "sole of a shoe." The second and seventh are directed more laterally than those intervening. Each foramen is bounded above and below by a pedicle, in back by the posterior articulation and in front by vertebral bodies and the intervertebral disk.

In the oblique view of the normal cervical spine, all arches, as well as the foramina, pedicles, and vertebral bodies appear in a smooth, sweeping, symmetrical curve about equidistant from each other. Any malalignment in this curve or irregularity in the spacing of the sections indicates a disturbance in the structure or the articulation of the cervical units. The dorsal spinous processes should be just visible at their tips behind the spine and the angle of the jaw usually crosses the second vertebra. (Figures 10 and 11.)

The pedicles on the side opposite to the visualized foramina, that is, the side farthest from the film, appear as a curved line of small equidistant oval shadows one for each vertebral body. If correct technic has been used in positioning the patient this line of pedicle shadows will intersect the shadows of the vertebral bodies near their anterior

Figure 9. Oblique view same patient as Figure 8. Foramina 3, 4, and 7 normal. Foramina 5 and 6 encroached upon by the exostoses seen in Figure 8.

surfaces. The interpedunculate distance represents the size of the foramen. In certain cases of cervical spine disturbance, these pedicle shadows may be distorted in shape, size, spacing, or alignment or in cases of advanced disk degeneration they may be obscured by demineralization or the overlying shadows of exostoses. (Figure 5.)

Disk Degeneration (Geredisk)

At the apices of the spinal curves, that is, the mid-cervical, mid-dorsal, and lower lumbar regions, the spine is placed under its greatest functional stress. It is likewise at these levels that the earliest, and later, the most advanced, stages of disk degeneration are visualized—apparently as a direct result of the wear and tear of use. (Figure 12.) In the mid-cervical region this corresponds to the level of greatest amplitude of the gliding movement. (Figures 6 and 7.) At first, the changes are seen on the concave side of the curve, that is, the more compressed side of the disk. In the dorsal region this is anterior while in the cervical region the posterior portion of the disk first shows degenerative change.

Figure 10. Normal 45° oblique view. Cervical bodies 2 to 7 with their foramina, pedicles (P), and laminae (L) appearing in a symmetrical curve. The four arrows indicate the third, fourth, fifth, and sixth intervertebral foramina. Note their size and shape.

Figure 11. The same patient, same view as Figure 10 but with neck held in extreme dorsal extension. Note the same intervertebral foramina indicated by the four arrows have become markedly constricted by extension of the neck. The vertebral bodies, pedicles, intervertebral foramina, and laminae all appear in a symmetrical curve.

This wearing out process begins as a replacement of the nucleus pulposus by fibrous tissue. The cartilage plates of the disk become fragmented and loops of blood vessels grow through these openings from the vertebral bodies into the disk substance. Later the disks become thinned. Bony trabeculae may form from this fibrosis either entirely within the disk or projecting from the vertebral body into it. (Figure 14.)

With thinning of the disks, the margins of the vertebral bodies impinge or approach each other. Thus bony spur formation or bridging is stimulated. Such spur formation about the disk or joint margins may project laterally, forward or backward into the intervertebral foramen or into the spinal canal.

Degeneration is not primarily the result of an infection or inflammatory process. Early disk degeneration will not show on the roentgenogram but when it has become sufficiently advanced it is seen as a thinning of the disk shadow with sclerosis of the vertebral plate, bony spur formation, and bridging.

The world "geredisk," to indicate the aging process by which it develops, is a better term than "degeneration" to describe this common condition resulting from the natural wear of life. The usual term osteoarthritis is inaccurate and misleading and should not be used. Arthrosis or spondylosis would seem to be more acceptable as the sections fail to show any inflammatory reaction.

Foramen Encroachment

There are at least six ways in which intervertebral foramen encroachment may occur.

The first is physiologic. The foramen is constricted by dorsal extension or by a permanent lordosis increasing the normal cervical curve and causing the superior articular processes to extend into the upper portion of the foramina. (Figures 10 and 11.)

Dorsal kyphosis exaggerates the cervical curve. Rotation or flexion toward the foramen also decreases its diameter and the opposite movements enlarge the foramen diameter. These facts may be useful in evaluating or eliciting a symptom.

Trauma, as fracture, or rarely posterior displacement of a cervical body may constrict a foramen. (Figure 15.) Although most displacements are forward, these tend to enlarge the foramen, but spondylolisthesis may constrict the foramen.

As stated above, an arthritic process involving the posterior joint with bony exostoses projecting

Figure 12. Specimen from cadaver showing destruction of fourth, fifth, and sixth disks. The second and seventh disks are essentially normal. There is an old traumatic angulation at the 3-4 level with fusion of the vertebral bodies and increased space between the neural arches. Compare with film of Mrs. J. S. in Figure 4.

Figure 13. Forty-five degree roentgenogram of cadaver specimen shown in Figure 12. The third and fourth neural arches (arrows) are separated as a result of the angulation. Intervertebral foramina numbers 4, 5, and 6 are encroached upon by exostoses projecting backward from the intervertebral disks. Foramen number 3 is somewhat enlarged by the forward angulation. Foramina numbers C2 and C7 are essentially normal. This is an advanced example of geredisk in a cadaver specimen.

Figure 14. Sagittal section from cervical spine shows a relatively normal fourth intervertebral disk. Normal cartilage plates CP visualized above and below. The nucleus pulposus (NP) and annulus fibrosis (AF) are intact anteriorly but deficient posteriorly at X. The anterior two-thirds of this disk is normal. A badly degenerated third cervical disk with cartilage plates fragmented: (1), the nucleus pulposus replaced by fibrous tissues (2), bony trabeculi (3), and new blood vessels (4), growing from the adjacent vertebral bodies into the disk substance. The vertebral bodies are nearly in contact at the posterior margins of the disk (x). This corresponds to the point of greatest compression stress on the concave side of the curve.

forward may cause foramen encroachment just as the bony spurs from the margin of a geredisk in front may project backward into the foramen. The spurs are much more extensive than they appear on the roentgenogram. (Figures 5, 9, 13, and 16.)

As I have previously described in connection with studies of the lumbar spine, thinning of the intervertebral disk from degeneration allows the bodies to come more closely together, producing not only encroachment of the foramen in a cephalo-caudad direction but also a certain degree of posterior joint telescoping subluxation. The inclination of the planes of the posterior articulations in the cervical region accordingly induces wedging of the superior articular processes forward into the upper portion of the foramina. This joint derangement may be a partial factor in causing the local pain, muscle spasm, and limitation of motion of which these patients complain. (Figure 5, foramen 3.)

Fibrous hyperplasia of the posterior joint capsule is a factor producing constriction of the foramen in some cases. Also in many of the sections studied intervertebral disk substance is clearly demonstrated bulging backward into the foramen.

Normally the nerve occupies about one-fifth to one-fourth the diameter of the cervical foramen; the remainder of the space is taken up by lymphatics, blood vessels, areolar and fatty tissue.

Bony or fibrous tissue encroachment may reduce the size of the foramen to one-fourth normal, crowding the nerve into the lower portion of the opening or it may become flattened in a ribbon-like manner or even completely destroyed. (Figure 16.) In examining cadaver material the nerve can usually be separated within the foramen by blunt dissection. In other cases it appears to be adherent and surrounded by fibrosis.

Patients with foramen encroachment not only complain of local pain, tenderness, muscle spasm, and limitation of neck motion, but also frequently suffer from radiculitis. (Figure 5.) In the cervical region this condition is characterized by pain referred to the shoulder, arm, or hand, corresponding in distribution to the involved nerve root and frequently aggravated by coughing or sneezing—the so-called Dejerine sign. Not all patients, however, suffering from radiculitis exhibit foramen encroachment on the roentgenogram.

Figure 15. A. (left). Traumatic subluxation of the fifth cervical body backward—reverse spondylolisthesis—with fracture of neural arch. Fifth disk thinned.

B. (right). 45° oblique view. Obliteration of fifth foramen (arrow) but the foramina above and below this are normal.

Figure 16. Roentgenogram of cadaver specimen with sections cut from four of the intervertebral foramina. Foramina 2 and 7 are normal in shape and size and show the section of the nerve occupying about one-fifth of the diameter of the foramen. The posterior articulations are seen to the right in these sections, and the intervertebral disks to the left. The fifth disk is thinned and there are exostoses projecting backward into the foramina from the fifth and sixth disks. This bulging backward of bony disk substance is visualized in those sections cut from the fifth and sixth intervertebral foramina. These openings are seen to be materially decreased in size and in the sixth one the nerve root is displaced downward into the lower portion. The fifth nerve root is completely flattened in a ribbon-like manner by the backward pressure of the bony spur formation projecting from the disk.

Figure 17. Spontaneous subluxation of the atlas forward on the axis incidental to cervical adenitis following rheumatic fever. Increased space between odontoid and the anterior arch of the atlas (A). There is an increased distance between the angle of the jaw (B) and spine. The spinal arch of the atlas (1) is well anterior to the normal curved line of those arches below it.

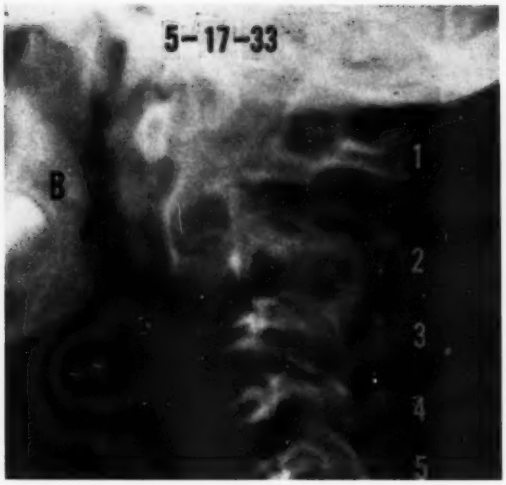


Figure 18. The same patient five weeks later, complete recovery following immobilization. The angle of mandible (B) is now in normal relationship to the spine and the first neural arch has returned to normal alignment with those below it.

Spontaneous Subluxation of the Atlas

Children complaining of painful stiff neck of sudden onset and without trauma should be examined for this condition. It usually follows an inflammatory process in the nasopharyngeal region, tonsilitis, or cervical adenitis. Most of the patients are children, although one of my patients was a man 33 years old with spondylitis deformans.

The spontaneous forward displacement of the atlas on the axis is thought to be due to a softening of the transverse ligament of the atlas or distention of the bursa between the odontoid process and the anterior arch of the atlas. The child may complain of painful torticollis and supports his head with the hands. He should be carefully handled since death has resulted from careless movement of the head in these cases.

On the lateral roentgenogram a widened space is seen between the anterior arch of the atlas and the odontoid process. The odontoid may be demineralized. The ascending ramus of the jaw is more than normal distance anterior to the spine. The posterior arch of the atlas is well anterior to the alignment of those arches below it. (Figures 17 and 18.)

Fractured odontoid process with forward displacement presents the latter two features but there is a history of injury and the anterior surface of the fractured odontoid is well anterior to the anterior surface of its vertebral body.

Here then are some of the common symptoms producing changes to be visualized on the various radiographs of the cervical spine. No attempt has been made to discuss severe trauma, disease, new growths, or congenital anomalies. The information to be gained, however, will repay a thorough painstaking examination of this region.

The Medical Bookman

MEDICAL ILLUSTRATIONS BY FRANK H. NETTER, M. D.*

THE work of Dr. Frank H. Netter has now become available in book form in the Ciba Collection of Medical Illustrations. This appears to be an excellent reference work for practicing physicians as well as an extremely useful teaching aid. It can also serve as a refresher course in pathology for general practitioners and specialists. An accomplished medical illustrator as well as a physician, Dr. Netter has combined normal and pathologic anatomy with histologic studies and clinical presentations of both common and rare diseases.

The illustrations are clearly and simply constructed, yet accurate in every detail. In the anatomical plates, color has sometimes been used arbitrarily but only to provide greater clarity and emphasis. For example, the arteries have been drawn in bright red and the veins in strong blue, an accepted practice in the portrayal of anatomy. In the paintings of pathology, however, pains have been taken to represent each structure realistically and to reproduce colors exactly.

Dr. Netter received his medical training at New York University and Bellevue. His interest in art remained strong, however, and he also studied at the National Academy of Design and took additional courses at the Art Students' League. While still a medical student he did a considerable amount of medical illustrating, but after completing his internship he entered private practice in New York. He was still much in demand as a medical illustrator, and finally decided to devote all of his time to these illustrating assignments.

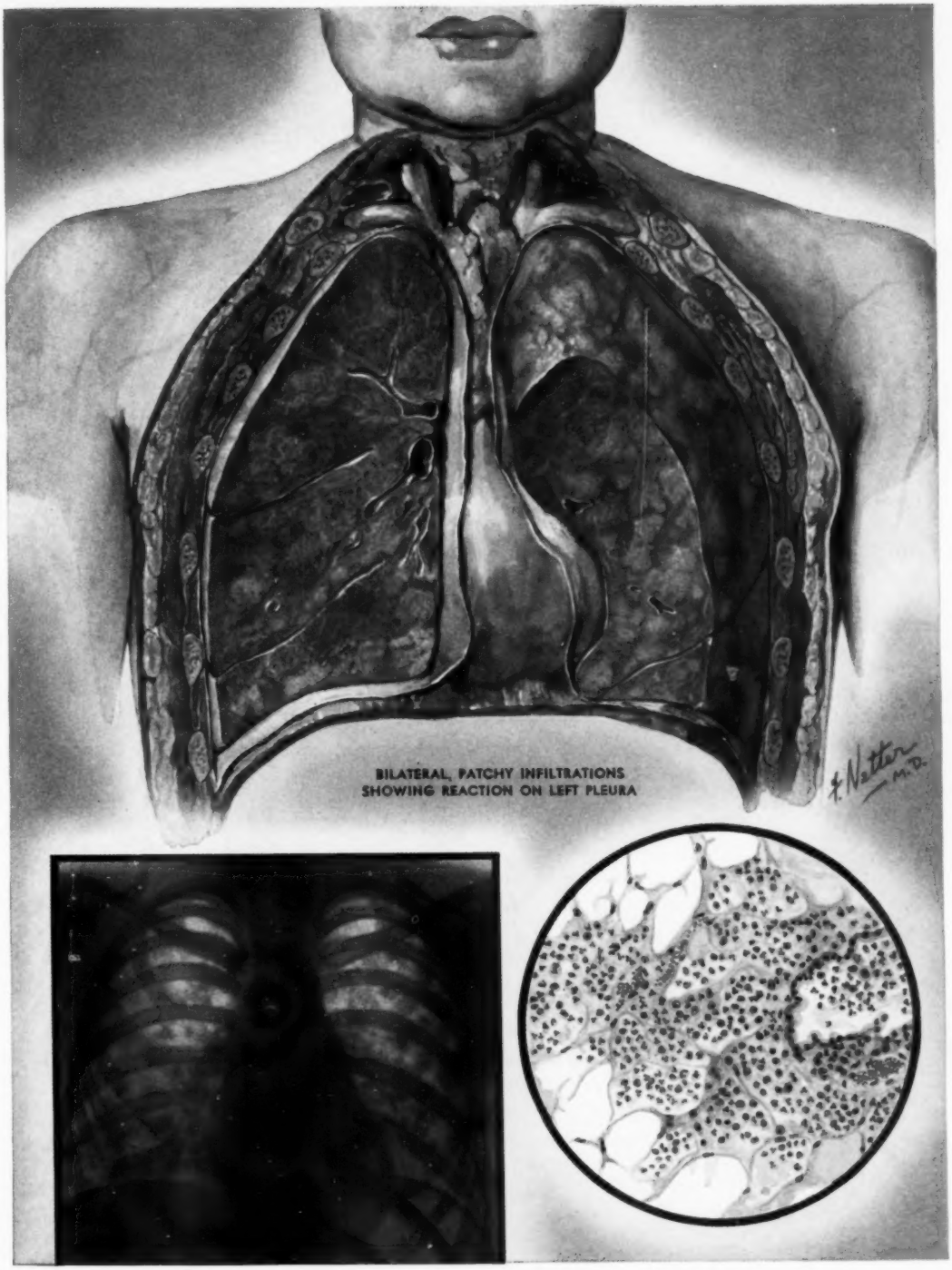
During the war, Dr. Netter was commissioned in the Army Medical Corps and illustrated many of the Army training manuals. After the war he returned to regular medical illustrating.

Included in this volume are the illustrations which for the past ten years have been distributed to the medical profession as separate sets of plates in portfolio form. Many of the individual illustrations are no longer available, but they are all to be found in this atlas along with many new plates. Originally, the portfolio drawings presented only the pathologic highlights, but later the normal anatomy was added and the work is being continued on this basis.

Wherever appropriate, Dr. Netter has used x-ray pictures with the drawings to provide better visualization of the internal condition portrayed. Full-color drawings of photomicrographs have been added to show the examination of pathologic conditions in a secretion or tissue.

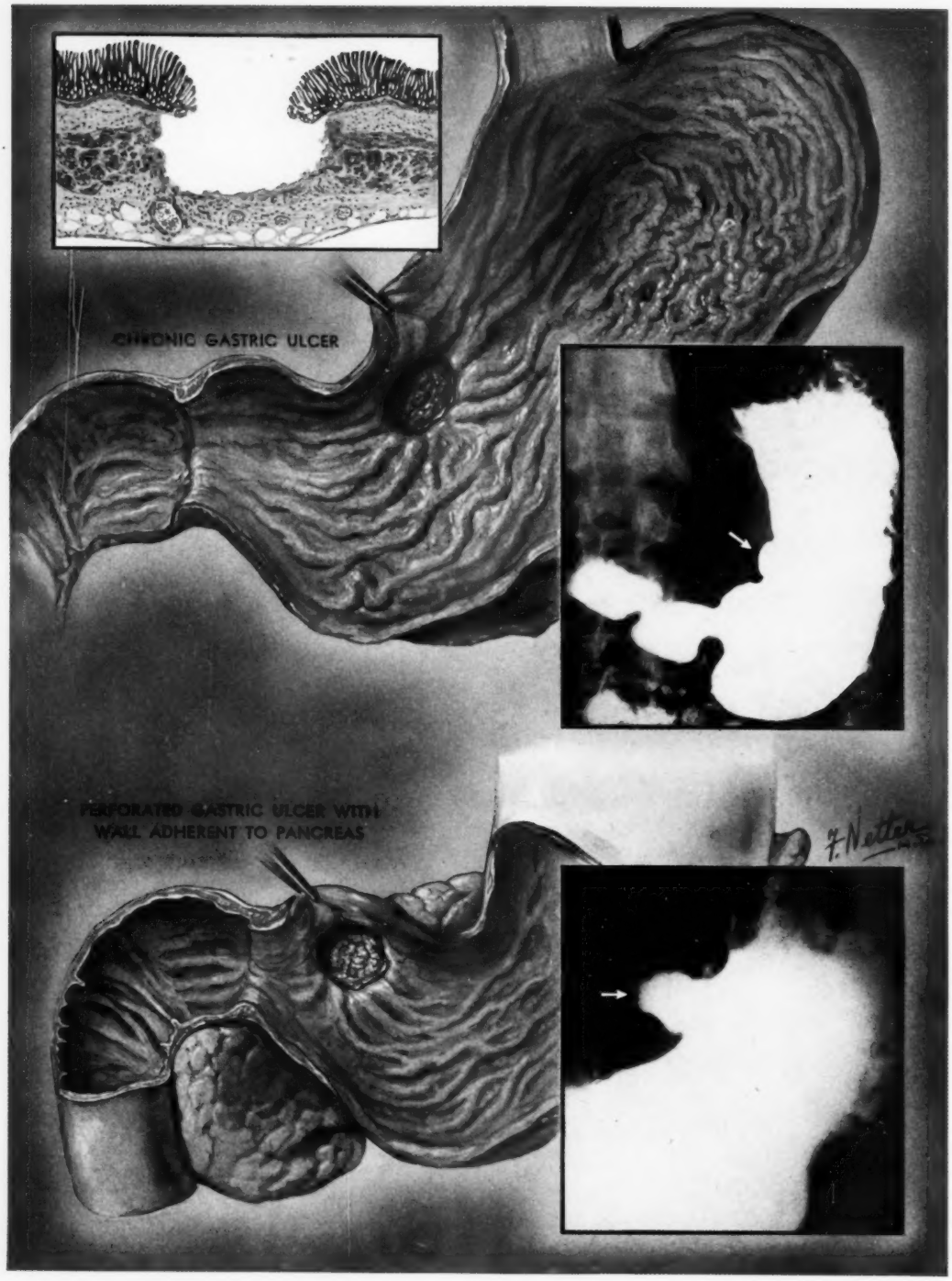
The book is divided into four sections: (1) Lungs and Chest, (2) Gastrointestinal Tract, (3) Male Reproductive Organs and Male and Female Mammary Glands, and (4) Heart and Aorta. The text accompanying each plate was prepared by authorities in the various fields. Among the authors are: Drs. Jacob Buckstein, Michael E. DeBakey, Charles F. Geschickter, Rueben A. MacBrayer, Henry H. Ritter, Eli H. Rubin, and Samuel A. Vest. Each section of the book is preceded by an introductory discussion which has been prepared by Dr. Netter.

*"The Ciba Collection of Medical Illustrations," by Frank H. Netter, M.D. 224 pages. 1948, Ciba Pharmaceutical Products, Inc., Summit, New Jersey. Price $6.50.



BRONCHOPNEUMONIA

Reproduction of the illustration from page 26 of
"THE CIBA COLLECTION OF MEDICAL ILLUSTRATIONS"



CHRONIC GASTRIC ULCER

Reproduction of the illustration from page 88 of
"THE CIBA COLLECTION OF MEDICAL ILLUSTRATIONS"

New Books Received

► PEDIATRIC ANESTHESIA - - -

By M. Digby Leigh, M.D., and M. Kathleen Belton, M.D. 240 pages, 84 illustrations. 1948, The Macmillan Company, New York. Price $5.50.

The striking developments in pediatric surgery during the past fifteen years have largely been made possible by the recent advances in pediatric anesthesia. Now, for the first time, Dr. Leigh's and Dr. Belton's accumulated experience with the problems of anesthesia in infants and in children has been assembled in an extremely readable and practical monograph.

The authors are fully qualified (as probably no other certified anesthetists are) to write on this subject. For a number of years, Dr. Leigh and Dr. Belton were director and assistant director of anesthesia at the Children's Memorial Hospital in Montreal. More recently Dr. Leigh has been appointed director of anesthesia in the Vancouver General Hospital and Dr. Belton has been made supervisor of pediatric anesthesia in the same institution.

The table of contents is misleading in its brevity. Yet within each of the thirteen chapters are detailed considerations of advantages and disadvantages of various anesthetics, of elective and emergency situations, of infants and children as different from adults, of methods of avoiding troubles rather than their correction once established. Perhaps the two most important principles emphasized are:

First, that the physiology of the infant is remarkably different from that of the older child or adult. Consequently special knowledge of the physiology of the newborn is imperative if ideal pediatric anesthesias are to be administered.

Second, that adequacy of oxygen is the No. 1 requirement in all anesthesia but it is especially difficult to fulfill in infants and children. Patients in this age group have high rates of metabolism with consequent rapid respirations and heart action. The margins of safety between adequate and inadequate oxygen supplies are much more exacting than in adults.

Considering the rapidity with which developments have occurred in the field of anesthesia it is to the authors' credit that the work is so closely up to date. The only outstanding omission is the satisfactory pediatric use of pentothal and curare as introduced by Baird.

T. C. C.

► DISEASES OF THE NOSE AND THROAT - - -

By Sir St. Clair Thomson, M.D., F.R.C.P., London, F.R.C.S., England, and V. E. Negus, M.S., London, F.R.C.S., England. 5th Edition. 1020 pages. 369 figures, 13 color plates, 20 radiographic plates and 11 other plates. 1949, Appleton-Century-Crofts, Inc., New York. Price $16.00.

Sir St. Clair Thomson died in January 1943, at the age of 82; therefore, this book is in the nature of a last will and testament. To it he gave all of his vast knowledge and experience acquired during fifty-five years in active practice. Those of us in America who were privileged to know and greet him here when he was a Guest of Honor of the American Medical Association, about 1913, will remember well how every word of discussion of papers and general conversation was touched by a saving sense of humor and the gift of literary eloquence. His intimate friendship with Mr. Negus (the latter refers to him as "my Patron") was most fortunate, since Negus was inspired by this great British laryngologist, and thus has perpetuated his teachings and much of his personality.

Major alterations are found in the chapters on malignancy of the eye, nose, and throat, and in treatment by the "newer remedies," penicillin, the sulfas, the antibiotics in general, and vitamins. Allergy and nasal physiology have been restudied in relation to sinusitis, and the displacement procedure of the American, Proetz, is given full consideration.

The chapter on "taking cold" is fused with a study of acute rhinitis, and a new chapter discusses sinusitis in children. An attempt is made to clarify "the confused subject of laryngeal paralysis." As for "direct tube work," full recognition is given to the Jacksons of Philadelphia and others of that school.

One may say that in this edition, much of value has been added and nothing of value has been omitted.

I. W. V.

► ATLAS OF PERIPHERAL NERVE INJURIES - - -

By William R. Lyons, Ph.D., Associate Professor of Anatomy, University of California Medical School; and Barnes Woodhall, M.D., Professor of Neurosurgery, Duke Medical School, Durham, N.C. 339 pages. 1949, W. B. Saunders Company, Philadelphia and London. Price $16.00.

This Atlas resulted from the experiences of the authors in World War II and the material in it was prepared while they were concurrently responsible for a heavy load of clinical and administrative duties.

In the 19 neurosurgical centers established during the war, many advances were made in various branches of neurosurgery, and particularly in the care of peripheral nerve injuries. The work on the controlled clinical material which was handled at these centers is incorporated in this unusual book. As Dr. R. Glen Spurling states in his introduction, the Atlas "develops an approach to acceptable peripheral nerve surgery which no other text in the field has heretofore developed."

The Atlas is divided into the following sections: (1) Introduction, (2) The Peripheral Nerve, (3) Completely Severed Nerves, (4) Traumatic Nerve Lesions in Continuity, (5) Nerve Sutures, and (6) Nerve Grafts.

Considerable space is devoted to illustrations of the alterations in tissue structure caused by the inhibiting influence of an advancing time interval between injury and repair. Also portrayed in detail are the use of different nerve wrappers and aspects of "early" nerve suture. Included in the introduction are descriptions of methods of fixing tissues and the clinical material used.

Painstaking care and skill have been lavished on the reproductions to provide unusually fine plates in both black and white and in color, together with a well-designed layout and printing job.

On the Contributions of ► HUGH OWEN THOMAS, SIR ROBERT JONES, JOHN RIDLON to Modern Orthopedic Surgery - - -

By H. Winnett Orr, M.D., Chief Surgeon, Nebraska Orthopedic Hospital, Lincoln, With a Supplement on Ridlon and His Share in Moulding Orthopedic Surgery by Arthur Steindler, M.D., Professor of Orthopedic Surgery, State University of Iowa Medical School, Iowa City. 253 pages, illustrated. 1949, Charles C Thomas, Springfield, Illinois. Price $4.50.

Although this book will probably appeal most to those engaged in the practice of orthopedic surgery, other readers will also find much to interest them in the account of these three pioneers.

Following rather brief biographical sketches of Thomas, Jones, and Ridlon, Dr. Orr discusses the principles and methods which Thomas, Jones, and Ridlon used and taught, quoting from their writings and including further events and incidents in their lives.

The book concludes with the chapter by Dr. Steindler on Dr. Ridlon's share in the development of orthopedic surgery, particularly in the United States. Both Dr. Orr and Dr. Steindler were pupils of Dr. Ridlon and credit him with impressing on them many of the fundamentals of their specialty.

► HUMAN BIOCHEMISTRY - - -

By Israel S. Kleiner, Ph.D., Professor of Biochemistry and Director of the Department of Physiology and Biochemistry, New York Medical College. 2nd Edition. 649 pages, 77 text illustrations and 5 color plates. 1948, C. V. Mosby Company, St. Louis. Price $7.00.

This book offers an up-to-date, comprehensive discussion of the physiologic processes of the human body. Starting with a section devoted to some of the basic concepts of physical chemistry, the text continues with chapters on dietary factors, body components and processes, metabolism of the dietary factors, and so on. Wherever pertinent, the author also takes up the pathologic as well as physiologic phases of the subject.

► NURSING CARE OF NEUROSURGICAL PATIENTS - - -

By Roland M. Klemme, M.D., F.I.C.S., F.A.C.S., Professor of Surgery, St. Louis University School of Medicine, St. Louis, Missouri. 117 pages. 1949, Charles C Thomas, Springfield, Illinois. Price $3.00.

This brief text is based on the author's lectures to nurses' classes and is directed to the nursing profession. Starting with a chapter on the anatomy of the head and spinal cord, the book goes on to discuss Clinical Signs and Symptoms, Neurosurgical Nursing Care of Head Cases, Neuralgias, Traumatic Head Injuries, Spine and Spinal Cord, Miscellaneous Neurosurgical Procedures, Scrub Nurse's Table—Materials and Supplies, and Instruments for Operative Procedures, and Special Procedures. Altogether the book should be helpful to the nurse who must know the special technics of a very specialized field.

► PSYCHODYNAMICS AND THE ALLERGIC PATIENT - - -

By Harold A. Abramson, M.D., F.A.C.A., Associate Physician for Allergy, Mount Sinai Hospital, Assistant Professor of Physiology, Columbia University, New York. 81 pages, 7 figures. 1948, The Bruce Publishing Company, St. Paul and Minneapolis, Minnesota. Price $2.50.

In addition to two articles by the author on the "Psychosomatic Aspects of Hay Fever and Asthma Prior to 1900," and the title subject, this book offers the first panel discussion on the role of psychodynamics and the allergic patient, arranged by allergists under the auspices of The American College of Allergists at its Third Annual Meeting in June 1947. The discussion considers the coordination of the principles of applied immunology and of psychodynamics and presents the viewpoints of authorities in the field of psychiatry as well as the problems of immunology.

► MAGIC IN A BOTTLE - - -

By Milton Silverman, Ph.D., Science Editor, San Francisco Chronicle. 2nd Edition, 386 pages. 1948, The Macmillan Company, New York. Price $3.50.

This book offers thirteen chapters in which are chronicled the stories of the more important and widely used drugs and the people who were responsible for their discovery and development. Mr. Silverman has managed to convey the drama and excitement, as well as the earnest and hard work, involved in the search for these agents in the fight against disease. He has covered the story of such well known scientists as Lister, Ehrlich, Fleming, Florey, and the Curies, along with the perhaps less famous but equally important achievements of men like Sertuerner, Pelletier, Withering, Koller and others who contributed much to modern therapy.

► HOW TO LIVE LONGER - - -

By Justus J. Schifferes, Recently Associate in Hygiene, Columbia College; Formerly Instructor in Health Education, Teachers College, Columbia University. 255 pages. 1948, E. P. Dutton & Co., Inc., New York. Price $3.00.

In this book, which is directed more toward the layman than the physician, Mr. Schifferes discusses the principal disease hazards which people in this country are most apt to encounter and points out the individual's responsibility for his own life and good health. Although the author interprets the possible meanings of various symptom complexes and the course that major illnesses usually follow, he makes no attempt at diagnosis or treatment, but recommends what sort of medical advice to seek, and describes the type of treatment that may be expected.

Men of Medicine

WILLIAM GERRY MORGAN

PERHAPS the best way to start the story of William Gerry Morgan is just this way: He is now 81 years old; he has held just about every position of trust and honor to which he is eligible; he is still practicing medicine, and he has no thought at all of retiring.

This *says* a lot, but it doesn't *tell* much. It lets you know that he is a healthy, disciplined man. It suggests that he has been president of the American Medical Association and of everything else on down. This is good enough for an introduction: good enough, because no introduction to Dr. Morgan would be quite adequate. He is not a spectacular man and he is not a simple man. Through half a century of service he has not revolutionized any field of science and he has not revolutionized any field of social relationships. Yet the sum total of what he has done for mankind and for medicine is, in a literal sense, almost beyond belief. He has been a busy man indeed. Physician and researcher; professional leader, writer and editor; Navy and Army officer; and, through it all, humanitarian. A highly-skilled and hard-working physician he is and was; no genius, no fool, no knave.

"I have just tried to do everything I could with what mental capacity God Almighty saw fit to endow me."

That is Dr. Morgan's self-appraisal. He gives it with modest pride, but without modesty; he would like to have done more, and he'd not be satisfied with much less.

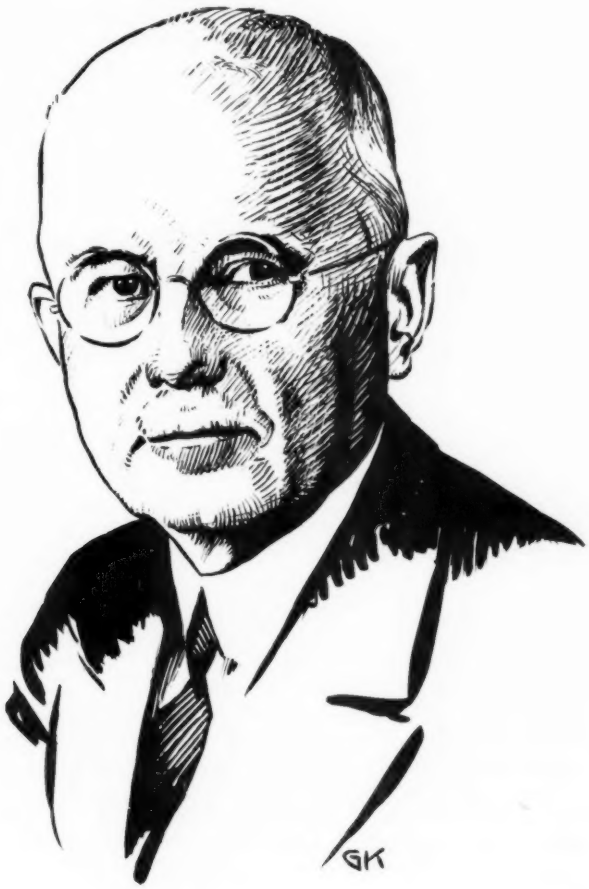
For the last half century—twenty years in the same building—he has practiced in Washington, D.C., specializing in gastroenterology. The offices which he shares with an associate and assistants are well equipped. His private office is about 16 feet square. The wall facing his desk is packed solid with framed degrees, citations, certificates of office, and notations of honors—48 of them. Crammed into Who's Who, part of the story they tell takes 32 lines. Windows occupy one wall. The other two—behind his desk and to the left—are packed with other framed remembrances—photographs, the usual thing, each with its few words of affectionate friendship. About half of these portraits look familiar to any visitor. You think you've seen them before. And you have. General George S. Patton, pearl handled pistol and all; Calvin Coolidge, Woodrow Wilson, William Howard Taft, senators of today and yesterday; admirals, actors, actresses, ambassadors. "Oh, no. They weren't all my patients. Some were, yes. Wilson, up there at this end, he was never a patient of mine . . . and some of the others, just friends."

That is about all from Dr. Morgan on the portraits. He says he has plenty of little stories about them—anecdotes—but these he keeps to himself. "I don't think it's up to me to talk about these people."

When William Gerry Morgan went into practice in Washington, D.C., in 1899—just at the end of the Spanish-American War—it wasn't an experiment. He knew that was the city for him and that he'd live out his life there. He had been out of school long enough to decide a few things for himself, and a few things more important than geography. To decide them definitely and finally.

For one thing, he knew he wanted to practice internal medicine. He had seen enough of general practice, his own and others, to realize that surgery wasn't the one great cure-all.

"In those early days," he says, "I used to hear surgeons say 'Well, let's go in and have a look at it.' That idea used to haunt me at night. . . . 'Let's go in and have a look at it.' Weren't you supposed to learn what was there—to *try* to learn anyway—by a correct diagnosis? What was happening to the art of medicine?" So, more than fifty years ago, before he came to Washington, Gerry Morgan had made this decision: He would learn everything he could about internal medicine, he would



WILLIAM GERRY MORGAN

become the best diagnostician he could "within the limits of my capacity."

The young man had made another decision, too. He had, as far as anyone can, realized that if life were to have any meaning at all for him, he would have to live it by certain self-imposed rules. "I can remember clearly when I first started to think about any purpose in life," he says now. "I was nine then, but I remember everything about that day. I was in Maine, at Freyberg. It was summer and I was stretched out under an oak. Blue was my favorite color, and it was a beautiful, clear day, with lots of blue in the sky. I looked out through the branches and saw all that blue. Then, that particular day, something became clear to me. I thought 'God has been good to me. Today He's even put all that blue in the sky.' "

Seventy years later, Dr. Morgan stood erect from his desk as he talked about that day. He walked over to the window, looked out into a dismal, rainy Washington afternoon. "So it was clear to me that day. God was good to me. And the only way I could go on into life and enjoy living was to live so that I'd always be wanted. Not the love of my family, although I've been blessed with that. But to earn the respect of other people by helping them and trying to understand them. Maybe I'd have come around to that idea anyway. But the blue in the sky I remember—that was what made it all so plain to me."

That wasn't the only rule of conduct that young Dr. Morgan brought with him to Washington. Another was personal discipline, a methodical approach to every situation. He picked up a prescription pad, a usual type, with carbon paper. "You know, I started this in Houston—that was in 1894. Then no one kept a copy of prescriptions. Well, a friend of mine didn't either. But once the druggist made a mistake. There was a lawsuit and the druggist said the prescription was in error, but that he'd lost it. The patient collected damages. So I started keeping copies of prescriptions from that day."

Dr. Morgan reached in his desk and found another bit of evidence, a large cardboard sheet, ruled off and lettered with small, clipped notes. "Date, weight, suit, underwear, shoes," were the headings on the columns. "Every week as far back as I can remember I've weighed myself. I know what the suits, shoes and other things weigh, so I can always tell just what I weighed. And of course I use the same scales each week."

Another product of this methodical approach is a "one-sheet" chart for each patient, with every treatment, every important fact, including laboratory reports, noted in abbreviated form. "As far as I know I started the use of this system. It must help others, too, because I've seen a lot of them using this or something like it." Of course he's kept a diary; he started it when he entered Dartmouth in 1886, and there are few, very few, days missing in the sixty-three years since that date.

So much for purpose and discipline. But there is one more Morgan rule. "I may be a little stubborn," he says. "I suppose I am. I decided when I was still a young man—before I came to Washington—that I would not be dominated by anyone or anything. I wouldn't let people or events pull or push me in any direction I did not of my own choice decide to go. Of course I've had to pay a penalty for this now and then . . . I can remember a few times when I've had to hurt others . . . and when I've had to hurt myself, deeply."

RARELY does any man rise far without the friendship, the guidance, the stimulation of another, usually an older man, one who sees in the younger a character and a mind. Dr. Morgan's sponsor is a name known the world over in internal medicine. He is Dr. Max Einhorn of New York City. Dr. Einhorn now is about 90 years old; he's still a close friend of Dr. Morgan and between them a mutual respect and admiration has grown through the years. But don't mention botany; that's Einhorn's ardent hobby. Morgan says botany's all right in its place, but that one of the best things about nature is that it puts fish in the streams, bears in the mountains, and grouse in the brush.

The two met at Southport, Connecticut, a suburb of Bridgeport. Dr. Morgan was practicing at Southport, a general practice with the general practitioner's surgery. For Dr. Morgan, Southport was the second stop. Out of Dartmouth and the University of Pennsylvania Graduate School, he had first set up practice in Houston. "I suppose I'd be there yet, if we knew then what we know now about malaria," Dr. Morgan says. "I contracted what was called 'Texas Fever.' My doctor did what he could, then he told me I'd have to leave Texas to get away from the climate. Now we know what 'Texas Fever' is: it's a form of malaria. If we'd treated it with a quinine preparation, if we'd applied the same rest and supportive treatment we use now—well, I might still be in Texas."

At Southport, the hard core of Dr. Morgan became evident. It was there that he laid down for himself this rule: "A complete and convincing diagnosis must be arrived at before I will operate or before I will permit another to operate on any of my patients." This meant, automatically, that he would have to have help, a consultant more versed in internal medicine than himself. When he selected this outsider, this consultant, there must have been a goodly patch of blue in the sky. The outsider was Dr. Einhorn, already world famed, who came up to Southport over week ends.

The next step seems quite natural. After a few months of these week end consultations, Dr. Einhorn made this proposition: "Why don't you make your break now while you're still a young man? Why don't you go into internal medicine exclusively? I want you to spend two years working with me in New York. Then, if you haven't made a mistake in this decision, I suggest you make Washington, D.C., your home. There'll be work for you there."

It all seemed logical and natural, but was anyone being dominated in this arrangement? "I don't think so," says Dr. Morgan. "You see, I had already made that decision before Dr. Einhorn mentioned it; I was just waiting for him to make the suggestion. As to Washington, well, I thought that I'd have two years to think that over." Actually, a year's association was enough to convince Dr.

Einhorn that the young man was ready. And in the year, Dr. Morgan had decided on Washington.

Gerry Morgan was wealthy, the way that incomes were balanced up half a century ago. That meant that his son, as a young physician, had a distinct advantage; economic insecurity was no threat to him in those important early years of practice. And that advantage wasn't wasted. From the first day of his practice, Dr. Morgan was able to establish the ideal physician-patient relationship. "I have never known anything about my collections," he says now. "From the beginning, I've always been able to have someone else take care of my finances. I've not known who was paying his bill and who wasn't. To me they've all been people I was trying to help. If I'd walk into my bank today my banker wouldn't know me."

He was an only son and was always closely attached to his father. "I don't know why I wasn't spoiled; that is one of the things I'm constantly thanking God for."

That reference to God is not just phrase-making. Dr. Morgan is not using a figure of speech. He is referring to a Creator and a Controller. "I was brought up as a Congregationalist. But after a while I got away from that. I thought it was too much like so many other organized faiths. I don't see why mankind requires a strict ritual to get close to God. Why does a minister or anyone else have to talk for an hour or more to tell you a simple truth?"

But Dr. Morgan is a man of deep faith, in the simplest tradition. He says any accomplishment of his is due to the mind and the character with which God Almighty equipped him. And you know he means it just that way.

"No, I don't accept any strict definition of the Supernatural," he explains. "But I do believe in a Creator who controls the world and every living thing. I have an unshaken faith in a guiding force. Let me be more specific on that. It seemed to me that, in research and in practice, as we learn more about the human body we think we move out in a strange new direction, and I suppose we do. Then, almost suddenly, we're back in a familiar area; it seems to be all part of a pattern. We're not too inclined to recognize this as we go along, but I know it's there. I know that now. No, I don't see how a physician can be an agnostic."

If the father gave him security, he also left him responsibility. The elder Morgan's income came from an industry that hasn't existed for many years, the manufacture of wooden shoe pegs. They were made of white birch and maple, Dr. Morgan recalls. He should remember something about that business, because he ran it for five years, along with his growing practice. That was immediately after his father's death, while there was still a factory to manage. Years later fire closed out the business for good. It wouldn't have had long to run anyway; machine stitching had arrived.

But those five years of being manager and physician were good training for the crowded years ahead. The time, for example, when Dr. Morgan was dean of Georgetown's Medical School, a regent of the university, a professor of internal medicine and, of course, a practicing physician—all at the same time. Dr. Morgan keeps one daily reminder of his years as a manufacturer. It's the cable address, "Germorgan," still printed inconspicuously on his letterheads. "Just before the factory burned down," he explains, "We had a pretty good export business in Germany, and other countries upon the continent as well as all South American countries."

For a quarter of a century and more, while the three Morgan daughters grew up, went to school and moved out into Washington's social life, there was much activity—"extensive entertainment," Dr. Morgan admits. For Dr. Morgan these were also years of tremendous professional service. Professor, dean, editor, researcher, and during this period president of six national associations. Now Dr. Morgan says, "Perhaps I should have tried to accomplish more in research, that's so important and so needed. But, then, would I have had time for the rest? I don't know." One of his research developments, promising then, is almost forgotten now. It was the "gastrodiaphane," an arrangement for dropping an electric light bulb into the stomach and cooling it by means of water circulating within a glass jacket. For a short time there was a flurry of excitement; the Army and Navy ordered a number, and it appeared to solve a great problem. Then the x-ray rapidly came into use, followed by the gastrograph. So the "gastrodiaphane" could be retired.

On this, Dr. Morgan was not too far ahead of his field—just a year or so. But that isn't typical. In 1904 he delivered an address before a local medical society on the subject, "Diagnosis and Treatment of Pernicious Anemia." His concluding

paragraph reads: "We do not know the cause of pernicious anemia. From a close observation of this disease I have learned that the juiceless state of the stomach is not the cause of this disease, but rather the result of whatever it is that does produce pernicious anemia. I have the settled conviction that the cause must be sought in the upper right quadrant of the belly, either in a disturbed function of the mucosa of the duodenum or of the gallbladder. So, too, we do not know the causes of cancer. I believe that cancer is not caused by infection but rather by a disturbed condition of the nerves supplying the cells which go to make up the cancer nest." That was fifty-five years ago. If it wasn't a completely accurate observation on these two widespread diseases, it was skirting very close to what is known today.

Again in 1921, in addressing a medical society, Dr. Morgan put into one paragraph his summary of the challenge to medicine. It would not be notable except that today, almost thirty years later, it is just as applicable. He said: "Among the more pressing problems which face the medical profession today is the discovery of the cause of cancer; a more perfect control of tuberculosis, leading to its ultimate eradication; the ultimate elimination of venereal disease through compulsory registration, and a wider dissemination of the knowledge of these diseases among the laity; also a more accurate knowledge of the etiology, pathology, and care of epilepsy."

Just a few examples of how Dr. Morgan accepted his responsibilities of office: During the time he was president-elect and president of the American Medical Association (1930-1931) he traveled 52,000 miles and visited every city of more than 100,000 population. During this time also he wrote almost 50 articles. They ranged from "Some Observations on Etiology and Prevention of Disorders of the Digestive System," to "Shakespeare's Knowledge of Medicine." The latter reflects another of Dr. Morgan's interests, enjoyment of good literature.

In those years, prohibition was the white hot issue in this country. As President of the American Medical Association, Dr. Morgan's views were sought out. He could have dodged the issue, but he did not. He spoke out freely; he was against prohibition, not because he enjoyed alcohol, but because he considered that the law itself was in interference with the individual rights of the citizens and an offense to the professional freedom of the physician. Here is one excerpt from his personal campaign against this law: "Faddists of every type are the curse of modern civilization, and though each in turn is but short lived, yet there is always another to take his place. It is a curious psychological fact that the failure of one fad after another to satisfy the needs of the gullible public does not even sufficiently assault their intelligence to cure them of the fad habit." Another time the direct attack: "I wish to say that I am unalterably opposed to the requirements of the Volstead act that upon the stub of the prescription blank shall be written the name of the disease of the patient with the accompanying right of inspection of it by some roving federal agent."

Even then, the question of a compulsory federal health law—socialized medicine—was the most important long-range issue facing the American Medical Association. In carefully weighed words, the A.M.A. president stated his views. He said simply: "If socialized medicine arrives, it will be because the doctors have failed to cover their field properly, have failed to carry out their responsibility."

Looking back on his leadership in a score of organizations, Dr. Morgan says: "The American College of Physicians today is the outstanding association of internists. Of everything I've done for organized medicine, I'm proudest of my contributions to it. I'm grateful that I had the opportunity to help in organizing it. With Dr. Heinrich Stern and Dr. Webb Wilcox and several others, I helped to found the College of Physicians in the early nineteen hundreds. I've served it in many ways, and eagerly, but I've never been president. When I was young enough and active enough, the college did not then see fit to ask me. Later, well, then I knew I couldn't do the job the way I would want to do it." That suggested the question: What is the ideal age for any man to take over such a responsibility?

"There is no ideal age. I believe the only requirement should be experience and comprehension; that a man should be a member long enough to understand the past, present, and future of the organization; that he should know its past problems, its present operations and its future objectives. Given this in a president, I don't think it makes much difference whether he's 35 or 65 years of age."

Dr. Morgan believes he couldn't have carried

these heavy loads without the complete cooperation of his associates. He's proud not for what they have done for him alone, nor for their own individual achievements, but because they've always been a team. He notes the fact that his present associate, Dr. William Ballinger (President-elect of the Washington, D.C., Medical Society), has been with him for twenty-five years. That quarter century of service seems to be another rule. Two nurses in his office have been with him more than twenty years each. His private secretary, Miss Julia Donohue, retired last July after forty-three years of continuous service. All this time she was also his financial manager; this assignment she still carries out, even in retirement. "And would you mind mentioning also that I've had the same chauffeur for twenty-five years?"

The fact that for so many years he's been associated with and has shared in the progress of internal medicine is, of course, Dr. Morgan's greatest satisfaction. "I have an example quite close to me," he says. "Our first child was a boy—he died before he was three. It was dysentery, tropical dysentery, contracted from a maid. Then we just didn't know enough about it. Now, I'd know what to do. I think that now he could have been saved."

Dr. Morgan believes the greatest progress has been made in the diagnosis and treatment of ailments, particularly the infectious diseases and syphilis and pneumonia. Half a century ago treatment for pneumonia was mostly supportive, using external heat "and trusting to the strength of the individual and his ability to throw off the sickness." Now sulfa drugs, penicillin and more vigorous feeding technics play their great roles.

"Even with something like virus pneumonia, where there's no absolute cure known now, we've come a long way," Dr. Morgan says. "When I started practice we called it *capillary bronchitis;* and around hospitals it was known as 'the old man's friend' because older patients seldom recovered from it. Now, we recognize it for virus pneumonia: we don't know all about it, but we can treat it."

Mrs. Morgan is the former Cora Boyd. Her father, John Boyd, was a Washington representative of the Southern and Central Pacific railroads. In the Civil War he had been close to Abraham Lincoln, one of the small group of men with a "know-how" about the industrial war-making capacity of the north. As a girl, Cora Boyd had two avocations, horses and singing. "She had a good voice, a very good voice," Dr. Morgan says. "But it wasn't good enough for opera singing or anything like that. So this was never an issue."

However, Miss Boyd did make an issue of horses, and she won her point, very early. She decided that a man should never be without a good riding horse, and her man never has. Right now the Morgans have two riding horses at their New Hampshire farm. Dog breeding is another hobby that hasn't faded with the years; 40 or 50 English setters keep the horses company.

Among the grandchildren, there's a probability that there will be one physician. He's Gerry Hardison, who is interested in medicine and is preparing to enter Dartmouth College. However, if the Morgan family wanted to staff a small Navy task force, it would have three admirals ready to take command. The daughters have all gone Navy.

If this chronology, this placing of a few milestones in a career, makes William Gerry Morgan appear at all stuffy, that is a mistake. He's known the drawing rooms of Washington and Europe, and lecture halls all over the nation. But he's also been quite comfortable with a week's beard, hunting and fishing and just exploring from Alaska to the Gulf of Mexico. In 1927, when the records show he was almost 60 years of age, he took a pack trip deep into Alaska, making camp at one time just 12 miles from the Arctic circle. But his favorite sport is "white water" fishing, a New England term for fast rivers and streams where you find the best trout and salmon. He's taken bass in most of the northern states, a few sailfish off the coast; tuna, hard heads, blues and trout in the nearby Patuxent River and Chesapeake Bay. Wild geese on the Potomac and wild turkeys in the southwest. Now, he'll settle for grouse shooting at that farm at Springfield, New Hampshire, just 20 miles from his old school, Dartmouth. He'll also go over occasionally to see one of his neighbors, Dr. Max Einhorn. He'll remind him that botany is all right as a hobby, if kept in its place.

George E. Connery

EDITORIALS

COMPOUND "E"

What appears to be a new approach to the treatment of rheumatoid arthritis is contained in the recent announcement by Drs. Philip S. Hench, Edward C. Kendall, Charles H. Slocumb, and Howard F. Polley of the Mayo Clinic.[1] After some twenty years of intensive investigation, a new substance, called "compound E," which seems to show significant promise in the treatment of rheumatoid arthritis, has been synthesized.

The new substance is an adrenal cortical hormone, known in the laboratory as "17-hydroxy-11-dehydrocorticosterone," or by the shorter name, "compound E." After a long series of complex biochemical investigations carried out cooperatively by Dr. E. C. Kendall and his associates of the Mayo Clinic, and by chemists of Merck & Co., Inc., Rahway, New Jersey, partial synthesis of what is now known as "compound E" was achieved in 1946. The excessive rarity of compound E for some time to come arises from the fact that the starting material must pass through more than 30 intermediate steps which can be carried out only by experienced chemists. Production of the compound on a large scale will require many months before manufacturing processes can be developed.

Search for the drug now known as "compound E" began in 1929, when Dr. Hench noticed that arthritic patients reported inexplicable relief of pain when they became jaundiced, and that women with arthritis likewise were relieved of arthritic pain when they became pregnant. Coupled to these observations was the known fact that rheumatoid arthritis itself sometimes is dramatically halted, with no apparent explanation. This led to the concept that "within every rheumatoid patient corrective forces lie dormant, awaiting proper stimulation." The agent which would produce such stimulation was not known, but it was believed to be a biologic compound specific in both nature and function. As an unknown factor, this agent was given the name, "antirheumatic substance X."

Next, it had been noticed, incidentally, that in some cases, rheumatoid arthritis was temporarily relieved when an arthritic patient underwent anesthesia or a surgical operation. During such procedures the adrenal cortices, which are the outer layers of the adrenal glands, lying at the upper end of each kidney, are stimulated. It was therefore suggested that anesthesia or surgical operation might stimulate the adrenal cortices to produce a certain hormone which would, in turn, exert a beneficial effect on rheumatoid arthritis. Hence, as early as 1941 Drs. Hench and Kendall speculated that the unknown "antirheumatic substance X" might be a hormone produced by the outer layers of the adrenal glands situated in close approximation to the kidneys.

Finally, after many complicated laboratory investigations by Dr. Kendall and chemists of Merck & Co., Inc., compound E was evolved in 1946. It was not available from the manufacturing chemists until September 1948, and even then, the supply was so infinitesimal that continuous or routine treatment of patients with rheumatoid arthritis was impossible. The use of compound E, therefore, was and still is considered to be in the nature of investigation of its properties.

The first patient to receive compound E had rheumatoid arthritis so severe that no form of

[1]Hench, Philip S., Kendall, Edward C., Slocumb, Charles H., and Polley, Howard F.: The effect of a hormone of the adrenal cortex (17-hydroxy-11-dehydrocorticosterone: compound E) and of pituitary adrenocorticotropic hormone on rheumatoid arthritis; preliminary report. Proc. Staff Meet., Mayo Clin. 24:181 (April 13) 1949.

treatment had aided her. On the day she first received the compound she could scarcely get out of bed. No significant result was noted on that day. On the third day, however, she was up and out of bed, walking with only a slight limp, and a week later pain and muscular stiffness had almost completely disappeared. She was able to go downtown and shop, the only result of this activity being fatigue.

Since this first patient was treated in September of 1948, 14 other arthritic patients have received compound E for varying periods. In every instance the stiffness of muscles and joints has relaxed markedly, pain and tenderness have lessened, and use of both joints and muscles has been significantly facilitated.

When the use of compound E is stopped, the rheumatoid arthritis returns after variable periods. Single or even a few doses will not permanently relieve the disease. In this respect Drs. Hench, Kendall, Slocumb, and Polley have warned that "much more experience is needed before we shall know how effective or safe the prolonged administration of compound E will be." Their report also places special emphasis on the fact that the manufacturers of the new substance will not be able to provide supplies of compound E until January 1950, and that even after that date the quantity of the drug will be exceedingly small.

J. R. E.

ARMED FORCES APPEAL TO GOVERNMENT-TRAINED DOCTORS

THE office of the Secretary of Defense a few weeks ago issued an appeal via individually addressed registered letters to all young physicians and dentists who received their professional training during the war under the A.S.T.P. and V-12 programs and who have not been in military service, to volunteer for duty with the Army, Navy, or Air Force medical services. The response to this appeal was disappointingly inadequate to meet the current needs of the Armed Forces.

The urgent registered letter appeal was in response to a proposal by the Armed Forces Medical Advisory Committee which had made a careful study of the medical officer requirements of the Army and Navy and had accepted them as valid.

Unless those physicians who will be eligible for release from military service this year are replaced by volunteers, undoubtedly it will be necessary for Congress to pass additional legislation to solve the problem. It is hoped, of course, that this solution will not be necessary.

Approximately 15,000 young men were deferred from military service during the war in order that they might complete their medical or dental training—many of them at government expense. Others were deferred to complete their educations at their own expense. It is felt that the 8,000 physicians who were not required to serve during World War II, and especially those who were trained partly or entirely at government expense, have a moral obligation to replace those men who have already served or who will be eligible for discharge this year.

To hold the medical officers now on duty beyond the period of two years of active service seems hardly fair, but this expediency may be necessary if endeavors to stimulate voluntary enlistments fail. In a recent editorial on the subject the *Journal of the American Medical Association* stated that "faced by these alternatives—a draft for those who have never served or the retention of those who have—the A.M.A. will no doubt urge the calling up of those who have not served."

In an effort to solve this seeming impasse, the Surgeon General early this year instituted a program to unite professional and civic support in every community behind the efforts to induce voluntary enlistments. The plan for civilian aid in procuring medical personnel has been developed in cooperation with the national organizations representing the professions involved and with prominent local officials and leaders.

A good share of the unwillingness on the part of the young men trained at government expense to volunteer is probably occasioned by

their reluctance to leave residencies which they hold at present. To circumvent this obstacle in the future, it has been proposed that hospitals give preference, in making their appointments to residencies, to those physicians who have completed military service. Such credit in competitive examinations often could be a determining factor in making the appointment.

The American Medical Association has also suggested that hospitals should review their contracts for residencies made for the next year. Where contracts have been made with men who have not had military service, the Association suggests that the hospital discuss the possibility of deferring the date for fulfilling the contracts and hold the residencies available until the physicians concerned have completed their periods of service in the armed forces. In the meantime, the hospitals should be able to secure as temporary replacements physicians who have completed their military service.

Furthermore, so that there will be no interruption in the professional training of the men involved, the services are willing to arrange so that those who volunteer now will be able to finish their current training periods before being called to active duty. It is also planned that calls to active duty will be so arranged that there will be a minimum of disruption in the civilian hospital training programs.

As the Secretary of Defense said in his analysis of the problem, ". . . men who saw no service overseas and who were not exposed to the rigors of war will themselves recognize our right to appeal to them to make a contribution in this emergency. From the ranks of these men we should obtain the replacements for those who have served and who are now entitled to return to civilian life if they desire.

"In a democracy, this procedure is fair, equitable, and just, and we propose to make our appeal to these former A.S.T.P. and V-12 students before taking more drastic steps."

A. E.

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OFFICE PRACTICE

Practical Procedures in Minor Gynecology

WALTER J. REICH, MITCHELL J. NECHTOW, AND M. WILLIAM RUBENSTEIN*

COOK COUNTY HOSPITAL AND GRADUATE SCHOOL OF MEDICINE, CHICAGO

THERE are many phases of gynecology embracing diagnosis and treatment that can be performed in the clinic or doctor's office. It may be generally stated that with ordinary precautions, relative mainly to asepsis and analgesia, many surgical-like procedures can be carried out in the ambulant patient. The use of local infiltration anesthesia of 1 per cent novocaine with or without a sedative barbiturate will allow for methods that would otherwise be carried out in a hospital. At the Cook County Hospital Gynecology Outpatient Clinic, the instruments and methods employed are, by necessity, the simplest possible. Some of the practical procedures carried out at this clinic will be presented.

PELVIC MALIGNANCY

Foremost among recent gynecologic advances has been the attack upon pelvic malignancy, with stress toward early diagnosis. Overemphasis cannot be given to the careful history, physical examination, and speculum inspection of the cervix. Since age is no true criterion for a diagnosis of carcinoma, especially of the cervix, suspicion should exist even in patients whose age falls below the erroneously so-called cancer-age group. An important step in early diagnosis has arisen from the liberal application of cytology and multiple punch biopsy.

The exfoliative characteristic of epithelial structures in general, and carcinoma in particular, forms the basis for cytologic search for the malignant cell. It is known that the carcinomatous lesion is the predominant type of uterine malignancy and that it occurs in the cervix about six to seven times as often as in the fundus. Of cervical carcinomas over 90 per cent are of the squamous type stemming from the squamocolumnar junction. The fundal or body carcinoma is a glandular or adeno type and arises from the endometrium.

The work of Papanicoloau and later, the work of Meigs, Ayre, and others have shown that cells with malignant morphology can be detected in smears taken from the vaginal pool. Subsequent work by Ayre showed that smears taken at the cervical os and from the squamocolumnar junction of the cervix furnished a clearer and even more fruitful picture of cellular structures, facilitating examination and recognition of the telltale cancer cell.

*From the Gynecological Division of the Cook County Hospital, the Fantus Clinics, and Cook County Graduate School of Medicine, Chicago.

Cytologic Examination—We have employed the Ayre wooden spatula for cytologic examination. A wooden tongue blade may also be used. Two different slides are smeared. The first application of the spatula obtains mucus material at the os as well as material from the squamocolumnar (erosio-intact) junction of the cervix. A rotary motion of the applicator with the cervix in direct view via the speculum affords easy access of smear material. Ayre's term "surface biopsy" may be well coined, for the cells are obtained directly from the cervical epithelium rather than from the gravitated pool in the posterior fornix of the vagina. The smears are immediately placed into a fixing solution containing half ether and half 95 per cent alcohol (ethyl or isopropyl) for a minimum of one-half to one hour.

"Write-on" glazed slides are used, and each slide separated from its neighbor in the fixative solution by use of a paper clip fastened on the superior (write-on) end. At no time should the slides be removed from the fixative and allowed to dry. If they are to be mailed, then upon removal from the ether-alcohol mixture, each slide (smear) is immediately flooded by glycerin and then covered by a separate dry (sandwiched) slide wrapped in paper or put into a slide box mailer. This glycerin method of Ayre and Dakin has proved quite satisfactory for further staining and examination, even if the slides are glycerin-covered for as long as seven to ten days.

Having obtained the material from the os (mucus), the partio and squamocolumnar junction of the cervix, a screening for carcinoma of the uterus can be carried out. Body carcinoma cells will in most cases (80 per cent) pass toward the cervical canal and adhere to the sticky mucus plug at the os. (From 10 to 20 per cent

of body carcinomas are missed by cytologic methods.) Cervical squamous carcinoma can be directly reached, as a rule, by the stroke of the spatula.

Biopsy—If the slides are positive for cancer cells, *biopsy* should be carried out. Several *punch biopsies* are taken from the most suspicious areas. As many as three or four can be carried out without anesthesia, as an office or clinic procedure. The areas to be punched are the suspicious ones plus the tissue at the junction of the normal and abnormal portion. Lugol's solution may be used here and will bring out this line of demarcation.

The tissue is placed in 10 per cent formalin solution for fixation. The biopsy sites are covered with Cotton oxycel, followed by a dry tampon. The latter should be removed in twelve hours.

A negative biopsy in the face of a positive smear read by one qualified in cytologic diagnosis may only require a second biopsy for confirmation. Very often a carcinoma in its very early stage is not only grossly invisible on physical examination but missed repeatedly on biopsy. We believe that in the near future greater emphasis will, no doubt, be given to the smears stained cytologically and read by one trained to read them. By such means, preclinical carcinoma, often pre-invasive carcinoma, will be more readily detected and, in turn, adequately treated.

ELECTROCAUTERIZATION OF THE CERVIX

Chronic Endocervicitis—A very effective yet painless method for dealing with chronic endocervicitis with eversion or ectropion is electrocauterization. Prior to cauterization, a cervical smear and/or biopsy is done.

The optimum time for treatment by electrocauterization is during the midcycle, in order to avoid possible bleeding. The latter can be avoided if: (1) care is taken that an accompanying acute or subacute cervicitis is *not* present, and (2) the degree of heat is not too intense. We have advocated a dull cherry-red of the common nasal tip cautery, as seen under ordinary illumination and not in the bright gleam of a directing light.

The "cold" cautery method is advised in order to avoid possible vaginal wall burns. Plain cold water is used for dipping the cautery tip before insertion in the vagina. The canal is cauterized circularly or at 12, 6, 3, and 9 o'clock and then the eroded surfaces are touched up. Canal cautery is all-important for it will destroy the diseased glands and epithelium, and thus prevent the outgrowth of the endocervical epithelium and its resultant ectropion.

Nabothian Cysts—These cysts are punctured by the cautery. Cotton oxycel is placed on the cauterized areas. A tampon is inserted to soak up any discharge and is removed within twelve hours. A disagreeable discharge is forecast. The patient is forbidden to douche or have sex relations for seven to ten days, in order to prevent breaking off the slough and possible bleeding.

The patient returns to the office weekly for about four to six weeks to assure postcautery canal patency. A simple cotton applicator or probe dilation of the cervical canal is performed at each visit. It takes about ten to twelve weeks for complete healing. Recauterization is rarely necessary and should not be done prior to three or four months.

Chronic Trigonitis—Some cases of chronic trigonitis, intractable to treatment, have responded well to cervical cauterization of a concomitant chronic cervicitis because of the contiguous lymphatic drainage of the cervix and the trigone of the urinary bladder. Hence the infected seat in the cervix will often exacerbate an already existing trigonitis.

TRICHOMONAS VAGINITIS

This is a very common cause of leukorrhea. Trichomonads can be detected by the hanging drop using warm tap water or normal saline. The mixture should not be thick. Staining is not necessary. Ordinary high dry power of the microscope will detect the moving trichomonads.

The following treatment is given: The vagina is thoroughly washed with diluted (1 to 3 of water) solution of liquid antiseptic detergent,* and then dried. Then through an open speculum (to avoid air embolism) 20 per cent argyrol powder in B lactose (40 per cent) and kaolin (40 per cent) (argypulvis)† is insufflated. The patient is given a sanitary napkin so as to avoid staining.

At home, daily douches (2 tablespoons white vinegar to 2 quarts of water) are used, followed by insertion of a 2 gm. argyrol compound (powder) (argypulvis) capsule deep into the vagina. To facilitate the action of the large capsule, three pin holes are made in both its ends: then the capsule is dipped in hot water momentarily, just prior to insertion.

If after a cure the patient returns with an active case, focal sites of reinfection must be checked. They may be the urinary bladder, Skene's ducts, Bartholin's gland, rectum, cervix, digital contamination, bedpan splash, or husband's prostate, prepuce, bladder, or urethra.

MONILIA VAGINITIS

This may be annoying, causing leukorrhea, itching, and dyspareunia. Because of the prevalence of vaginal glycogen during pregnancy, an excellent medium for monilia is created, and hence the frequency of this condition during pregnancy. White-gray plaques on the vulva, vagina, and cervix are seen. If wiped away they leave capillary-oozing sites. By use of the hanging drop, the morphologic characteristics of the thin, bamboo-like filaments of mycelia with buds are diagnostic.

*Parke, Davis & Company.
†A. C. Barnes & Company.

In treating the condition the plaques are washed off using the liquid detergent solution, and then painted with equal parts of 1 per cent aqueous gentian violet and acriflavin solution. This may be reapplied two to three times weekly or oftener if necessary. Care to prevent irritative reactions to the dye must be kept in mind.

Home care consists of sodium bicarbonate douches 2 tablespoonfuls to a quart of warm water. Pregnancy is no barrier to treatment. In some cases proprion jel‡ is supplemented as the home treatment, and nightly insertions for a week are of much benefit.

INTRACTABLE PRURITUS VULVAE

This is a most annoying entity. When etiologic conditions such as systemic, kraurosis vulvae, leukoplakia, trichomonas, monilia, or lichen planus, are ruled out, a so-called intractable pruritus vulvae exists. Frequently these patients have made the rounds to several doctors, dermatologists, radiologists, and even psychiatrists.

We have found that the subcutaneous, perivulvar injection of an oil has given unusually excellent results. Zylcaine§ is used. First, intradermal procaine wheals are made in each corner. Next, using an 18-gauge spinal needle, 10 cc. of the "oil" are injected into each of the labia majora, 5 cc. across the supraclitoric area, and across the rectovaginal septum. The hair is not shaved, and a simple soap and water cleansing is given.

Precaution that the injections are subcutaneous—at least 1 cm. below the skin surface—will avoid a possible slough. The patient is advised to take a tub bath within two to four hours. Relief is obtained within several hours as a rule, or it may be gradual, taking as long as eight weeks.

URETHRAL CARUNCLES

First, a surface or punch biopsy is done to rule out malignancy; then using 1 per cent novocaine periurethral block, electrocauterization with a fine nasal tip cautery will destroy the everted urethral mucosa and the para-urethral glands. Follow-up Sitz baths are advised, to minimize dysuria. Weekly urethral dilatation using a graduated urethral dilator or catheter is a very important part of this procedure. Often ascending trigonitis, cystitis, and bladder tenesmus are much relieved after adequate destruction of the urethral caruncle.

CONDYLOMATA ACUMINATA

These may be seen not too infrequently. These soft warts have been difficult to treat in the past, requiring anesthesia, surgery, or even radium. The application of 20 to 25 per cent podophyllin ointment in a hydrosorb base has been very effective. The adjacent normal skin and mucous membrane are protected by zinc oxide ointment or collodium. The podophyllin ointment must be washed off with soap and water within four to six hours. If left on too long the ointment will cause irritant reaction of pain and edema. P.R.N. application of any anesthetic ointment will make the patient feel quite comfortable.

The condylomata shrivel up and disappear in one to two weeks. Most cases require only one treatment. If another is needed, seven to ten days should elapse before application. Podophyllin is not effective on hard warts.

CHRONIC SKENEITIS

In order to eliminate the chronically infected seat in the Skene's glands, the latter must be completely eradicated. Electrocautery is best used.

The gland is strung up over a curved surgical needle, piercing the urethral lumen. A fine nasal tip cautery using cherry-red dull heat is then applied. Anesthesia is obtained by periurethral novocaine block. Prophylactic weekly postcautery urethral dilatations are done.

VAGINAL FISSURE

This condition most commonly occurs in the elderly patient with senile vaginitis. It is very painful. Treatment is difficult as a rule. We have found good results on the lateral walls when the surrounding area is (1) given prolonged anesthesia by use of subcutaneous Zylcaine in oil, and then (2) electrocauterized, using a fine nasal tip cautery. The anterior and posterior wall fissures are infiltrated with simple novocaine.

Supportive therapy with 1 mg. stilbestrol suppositories will aid in resistance to infection, cornification, and healing.

CHRONIC RECURRENT PELVIC INFLAMMATORY DISEASE

This condition, with its recurrent pelvic pain, menstrual difficulties, sterility, and occasionally its poor response to surgical treatment, will find marked improvement from intrapelvic (intravaginal) heat. The use of the Elliott or Thermoflo in daily treatments is employed. Each treatment lasts one hour at a temperature of 115 to 120° F. It is advised that the patient rest in the office after treatment for about one-half hour.

The number of treatments may vary from a period of two weeks to three to four months. Pelves that are rather fixed, and those that contain "fullness," sometimes "melt" away under just such therapy. Careful regulation of the temperature level will prevent vaginal burns.

It must be cautioned that these patients should not be explored soon after a course of treatment, in order to prevent handling of the hyperemic pelvic organs which may lead to peritonitis or even death.

We have found that a great number of patients cannot feasibly be treated as office or clinic patients because of either economic or time-consuming factors. For

‡Wyeth, Incorporated.

§Abbott Laboratories.

these we have been using a simple device, INTRAPELVIC HYDROTHERMY APPARATUS* that can be used at home by simply attaching it to the bathtub faucet. By means of a two-way flexible rubber hose mechanism, the hot and cold water blended to a suitable temperature will reach the vagina and inflate the intravaginal flexible rubber bag section.

This modified intrapelvic heat is taken daily in a reclining position with the bathtub partially filled with warm water, and best given for about one hour.

CERVICAL POLYP

Not uncommonly, small single cervical polyps are encountered on routine pelvic and speculum examination. They arise as a rule from a stalk in the endocervix. By a simple evulsion these polyps are easily removed, and as a rule, without any blood loss. The procedure is painless. As a safety factor it is followed by cauterization of the cervical canal, including the site of origin of the cervical polyp.

Attention must be given to the case of the cervical polyp that may look small and single, only to hide other (multiple) small polyps, each with its own stalk. Often pronounced bleeding will occur after these are removed because the bleeding sites may be high or even in the endometrium.

Care to differentiate an endometrial polyp from a cervical polyp is important. Usually the cervical polyp is brighter red, somewhat mulberry-like in contour, and its origin visible. The routine alertness for malignancy with the use of cytology and biopsy must be emphasized, again. Every polyp should be preserved for sectioning.

PRE-OVULATORY DILATATION

The recent studies on ovulation as determined by temperature graphs, "mittelschmerz," mucus-plug secretion, and cytology cornification level studies, have greatly aided in the determination of the probable ovulation period in the menstrual cycle.

In those cases of sterility that have remained recalcitrant in spite of the usual avenues of treatment and advice, we have occasionally found pre-ovulatory dilatation to be of value. Such procedures can be easily done in the office or clinic without anesthesia by the gentle use of uterine forceps or with dilatation by the smaller sized Hegar dilators. The use of cervical dilatation premenstrually, for those types of dysmenorrhea where cramp-like bearing down contractions are described, when all organic causes have been eliminated, has also been found of some value in our hands.

*Manufactured by the Clay-Adams Co., New York.

PESSARY

The best use of the pessary for the outpatient has been in the cases that have (1) malposition of the uterus with symptoms, and (2) procidentia occurring in a poor surgical-risk candidate.

In the first group the patient who presents herself with a backache especially during menstruation, who flows rather profusely, and whose uterus is retroverted or retroflexed, and hyperemic and whose broad ligament contains numerous large veins, can be greatly helped by pessary insertion.

Several factors, however, must be present before the pessary is used: (1) The uterus must not be fixed, and the pelvis must be free of carcinoma, endometriosis, and residual or subacute inflammation. (2) Other causes for backache and menorrhagia are to be ruled out, including the orthopedic.

The common type of pessary for correction of retroposition of the uterus is the Smith-Hodge type. The Gynefold modification (flexible lateral bars) facilitates insertion immensely.

The patient assumes the knee-chest position. A tenaculum is placed on the anterior lip of the cervix, and with a finger in the rectum pushing forward on the fundus and by traction downward and backward on the tenaculum, the corpus will usually be brought forward. The new position can be aided afterwards, bimanually, and the pessary then introduced so that the corpus is cradled by its posterior and lateral rims.

The pessary should be kept in place for periods of four to six weeks, removed, washed and then reinserted. The trial period for recto displaced uteri should not be less than two months, and if surgical correction is contemplated, adequate evaluation of symptoms with and without the presence of the pessary, should be made. If, in the younger individual, marked relief is received from proper pessary position, surgical correction may be considered.

SUMMARY

1. Fifteen common office procedures embracing gynecologic diagnosis and treatment are presented.

2. The widespread use of cytology and multiple punch biopsy is stressed, aiming toward early diagnosis of carcinoma of the uterus.

3. Treatments found efficacious for such common problems in gynecology as trichomonas vaginitis, pruritus vulvae, condylomata acuminata, vaginal fissure, and chronic pelvic inflammatory disease are discussed.

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Preview

Coming issues of POSTGRADUATE MEDICINE *will present these outstanding papers and scientific exhibits, as well as many other valuable and interesting articles, clinics, and special features.*

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Medical Aspects of the Death of Desdemona

IRVING S. COOPER[1]

MAYO FOUNDATION, ROCHESTER, MINNESOTA

In the three centuries that have passed since the death of Shakespeare, the plays of this "Soule of the Age" have been the wonder and delight of physicians. Sir William Osler advised each young physician to keep a copy of the works of William Shakespeare at his bedside. Dr. St. Clair Thomson,[1] in an address before the Medical Society of London, in 1916, said, "If any one of us today had to name the author which every medical man should study with diligence and delight, surely it would be the greatest of our great Englishmen, William Shakespeare. The science of medicine progresses, but human nature remains the same, and the foundations of physiology are fixed. Shakespeare's plays will be read by physicians when every medical treatise of the present year will have been completely eclipsed, and the works of this *master of medicine** will continue to be studied by future generations until 'there shall be no more death.' "

This interest of physicians in the Bard stems not only from the poetry of his writings, which "neither man nor muse can praise too much," but also from the wealth of medical knowledge which is found in his plays, and the consuming interest in disease and the practice of medicine which Shakespeare must have possessed to have enabled him to encompass all of the medical lore of this time. Dr. W. H. Witt,[2] addressing the Nashville Academy of Medicine, has admirably expressed the qualities that have particularly resulted in the special attention which physicians have devoted to the plays of Shakespeare. Dr. Witt said: "I have an opinion of him . . . as the one of all time who has plumbed the depths of human reactions and has given them the beauty of words, who grasped the essentials of all the scientific knowledge of his age. . . . His knowledge of the law has been openly adduced as a reason for doubting the accepted authorship of his works, and their assignment to Francis Bacon. We might as easily confuse him with a trained sailor, an apothecary, a musician; *much more easily claim he was a physician.*"*

Many others[3,4] have expressed the well-documented opinion that the knowledge of the medical practices of Elizabethan times possessed by Shakespeare and exhibited in his plays was equal to or surpassed that of most physicians in the England of the early seventeenth century and volumes have been written of the medical lore to be found in the plays of Shakespeare.[5,6,7] It is certainly evident to all that if others did possess the medical facts found in those plays, no poet recorded them as graphically or lucidly as did Shakespeare.

It is in this mutual interest of William Shakespeare and the physicians of three centuries in the respective works of each that this paper has its foundation. The case cited, the death of Desdemona in the tragedy of Othello, has previously been the subject of both literary and academic investigation, and is only one of many examples testifying to the truth of Dr. Thomson's statement that the works of this master of medicine will continue to be studied by future generations.

FURNESS' QUESTIONNAIRE AND THE REPLIES TO IT

The most striking example of the academic interest (both literary and medical) of physicians in the death of Desdemona is the questionnaire which H. H. Furness,[8] compiler of the "Variorum Shakespeare," sent to six prominent physicians at the turn of the present century, and the replies of these medical men to the queries posed.

It should be recalled that the death of Desdemona is represented as occurring in the second scene of the fifth act of "Othello." Othello, the Moor, has been deceived into a state of insane jealousy by Iago, who had treacherously and falsely, in the Machiavellian tradition, convinced Othello that Desdemona has been deceitful. The scene opens with the famous lines of Othello:

It is the cause, it is the cause, my soul;
Let me not name it to you, you chaste stars!
It is the cause. Yet I'll not shed her blood,
Nor scar that whiter skin of hers than snow,
And smooth as monumental alabaster.
Yet she must die, else she'll betray more men.
Put out the light, and then put out the light:
If I quench thee, thou flaming minister,
I can again thy former light restore,
Should I repent me; but once put out thy light,
Thou cunning'st pattern of excelling nature,
I know not where is that Promethean heat

*Italics are mine. I. S. C.

[1]Fellow in Neurosurgery, Mayo Foundation, Rochester, Minnesota.

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That can thy light relume. When I have plucked the rose,
I cannot give it vital growth again,
It needs must wither: I'll smell it on the tree.

Othello then openly accuses Desdemona of deceiving him and finally abruptly kills her. A moment later Othello hears a noise which he believes to be Desdemona reviving and he says:

What noise is this? Not dead? Not yet quite dead?
I that am cruel am yet merciful;
I would not have thee linger in thy pain.
So, so.

Emilia, Desdemona's servant and the wife of Iago, enters; Desdemona revives long enough to speak a few lines and then dies. Desdemona is later referred to as being as pale as her smock.

During the nineteenth century there was considerable academic discussion about this murder, the mode of its perpetration as conceived by the playwright, as well as the possibility of one reviving after apparent death so inflicted and speaking a few last lines before actually dying. However, since it would be beyond the scope of this paper, as well as beyond the ability of the author, adequately to discuss the multifaceted literary aspects of this question, it will be well to restate the questions sent by Furness to the physicians of his day, and to try to supply answers, in the light of physiologic

concepts at hand, to the medical aspects of Desdemona's death as represented in the play. Furness asked these physicians the following questions:

1. *Do you think Othello stabbed Desdemona when he said "So, so"?*
2. *If Othello had stabbed Desdemona could her smock be pale?*
3. *If she were smothered or strangled could she be pale?*
4. *In either case could she speak after apparent death?*
5. *If she could speak, why did she not quite revive?*
6. *From what cause, then, did she really die?*

Furness wrote as if the characters in the play were real and the death of Desdemona actual. This often-used device will be employed in the present paper. Opinions which Furness received in reply follow:

Dr. D. Hayes Agnew stated that death by strangulation would not be compatible with physiologic principles. He further stated that death by stabbing would not conform to the text. Dr. Agnew postulated that probably fracture of the larynx resulted in asphyxia, from which Desdemona partially recovered. He believed that death ensued because of shock, with spasm of the glottis.

Dr. D. G. Brinton replied that death by stabbing could not have been in the mind of the author. Brinton felt that the strangulation by Othello was incomplete, Desdemona dying from "cardiac exhaustion." He wrote that such cases are by no means rare and cited a case encountered in New York to give credence to his testimony.

Dr. J. M. DaCosta answered that Desdemona could not have died from the strangulation after having spoken her last lines. However, DaCosta stated that strangulation could have resulted in a pale countenance, and cited several recent cases to bear out his contention. He believed, however, that Othello stabbed Desdemona, after which she died from internal hemorrhage, thus enabling her smock to remain pale.

Dr. W. A. Hammond testified that Othello did not stab Desdemona when he said "so, so" but that he pressed her pillow forcibly against her face at that time. Hammond believed that, as a result of such an attack, Desdemona could have been pale in death but could not have spoken after apparent death. He further believed that Shakespeare was ignorant of the modus operandi of smothering.

Dr. William Hunt stated that he was happy to answer positively and at once that Desdemona died of fracture of the cricoid cartilage of the larynx, and offered a similar case, which he had recently reported, to lend weight to his diagnosis. He stated that the story of Desdemona's death is exactly in accordance with the ordinary sequence of symptoms in such cases, in which the patient is pale but can speak audibly though hoarsely, gradually succumbing to the pressure of edema and nervous shock.

Dr. S. Weir Mitchell answered that Desdemona could not have been strangled and died in such a manner as related by the poet, but that Shakespeare probably cared little for realism! Mitchell stated that death by stabbing would have made the sequence physiologically possible and that little blood on the smock would not have made less its general whiteness.

DISCUSSION OF THE REPLIES

In reopening this case for further evaluation, the primary question to be considered is the method in which Othello put Desdemona to death. Three ways have been proposed in which the jealousy-crazed Moor might have dispatched guiltless Desdemona. The three possibilities that have been suggested are: (1) that Othello stabbed Desdemona, (2) that he strangled her manually, or (3) that he smothered her with a pillow. The likelihood of stabbing can be ruled out by the earlier lines of Othello in which he soliloquized,

Yet I'll not shed her blood,
Nor scar that whiter skin of hers than snow.

Shakespeare was constantly striving in this act for the imagery of the effect of the pure whiteness of Desdemona compared to the blackness of the Moor. The only use which Shakespeare makes of color is in absolute contrast, and the spilling of Desdemona's blood would have lessened the intensity of this poetic imagery.* The opinion of S. Weir Mitchell in this regard is doubtless the one that is most far afield, and it is considered all the more surprising in view of the endeavors of Mitchell to combine both medical and literary efforts during his lifetime. It is difficult to credit lack of appreciation for realism on the part of a poet who described a winter scene with the lines (Love's Labour's Lost, V, 2):

When icicles hang by the wall,
And Dick the shepherd blows his nail,
And Tom bears logs into the hall,
And milk comes frozen home in pail.

Carelessness about realism is even more improbable when one considers the description of the death of Falstaff, which is described in the lines (King Henry the Fifth, II, 2):

. . . I saw him fumble with the sheets and play with flowers and smile upon his fingers' ends. . . .

That is a description of carphology which is as accurate as Mitchell's own word portrait of causalgia. Finally, then, Mitchell's thesis that Shakespeare cared little for realism cannot be accepted and the possibility that Desdemona was stabbed must be disregarded.

It is postulated that the stage direction, "He smothers her," which appears in some editions of Shakespeare was introduced by a producer later than Shakespeare's time. It is unlikely that Othello smothered his fair bride, inasmuch as he cried,

I would not have thee linger in thy pain.
So, so.

*Shakespeare's use of color is fully dealt with by Caroline F. E. Spurgeon in her book: Shakespeare's Imagery and What It Tells Us. Cambridge University Press, 1935.

Smothering is slow and torturous, and the emphatic words "So, so," would lead to the belief that Othello quickly terminated his grisly deed. The powerful Moor could readily have dispatched delicate Desdemona by strangulation and it is only this act which would be completely compatible with the text and with the ensuing events.

Therefore, it must be considered that Shakespeare intended that Desdemona die by strangulation at the hands of Othello. However, to pursue further Furness' inquiry: Is such a death physiologically compatible with the manner in which Desdemona died? And, finally, if it is physiologically compatible with the events, was Shakespeare aware of the realistic qualities of his description of Desdemona's death or were the physiologic facts beyond the ken of this "master of medicine"? Answer to Furness' query in regard to the pathologic results of Othello's strangulation of Desdemona requires brief review of this subject.

PHYSIOLOGIC ASPECTS OF STRANGULATION

Strangulation may result in death or unconsciousness in one of four ways: 1. The air passage may be shut off. 2. Pressure may be applied to the main blood vessels, resulting in the carotid sinus syndrome or cerebral anemia or both. 3. The phrenic and vagus nerves may be crushed. 4. Injury to the cervical portion of the spinal cord, with its ensuing chain of events, particularly paralysis of the muscles of respiration, may take place. Kemper and Gibson[9] recently reported two cases wherein children, accidentally hanged, both recovered following release from the noose. Minovici[10] once reported 12 cases of recovery following strangulation. In 1641, in a publication called "Newes From the Dead"[11] the following case of strangulation with recovery was reported:

> The victim was Anne Greene, a 22-year-old servant girl, ". . . of middle stature, strong, fleshie, and of an indifferent good feature." She was seduced by the grandson of her noble employer and was subsequently condemned to be hanged for murdering her illegitimate offspring. After a few distraught weeks in gaol she was ". . . turned off the ladder, hanging by the neck for a space of almost half an hour, some of her friends in the meantime thumping her on the breast, others hanging with all their weight upon her legs; sometimes lifting her up, and then pulling down again with a sudden jerk, thereby the sooner to dispatch her out of her pain." She was then cut down, and her body was placed in a coffin and taken to some physicians for dissection. When examined by them she was found to be still breathing and "to ruttle." An impatient and lusty fellow standing by who wanted to get to work stamped on her breast to end her misery. She "persisted to ruttle" even after this so they decided they had better attempt to revive her.
>
> Recovery was instituted at 9:00 A.M. of a Saturday morning. The attending physicians first wrenched open her mouth and poured "hot and cordial spirits" therein. This was followed by even more ruttling and coughing. They opened her hands, rubbed and chaffed her extremities, tickled her throat with a feather, gave her a warm enema and a mustard plaster to her chest. They decided to bleed her, but ". . . no sooner was her arm bound for that purpose, but suddenly she bent it, as if it had beene contracted by a fit of the convulsion." Her arms and legs were tied down, and she was bled on two different occasions, five ounces and nine ounces. That night she spoke intelligible words but was incoherent. Her pulse was very low (thready) and she had a fever the next day.
>
> On Sunday the patient ". . . lay often fighting and talking to herself, as if she had been still to suffer." Her throat was very sore; she had dysphagia and refused all fluids. She was feverish and euphoric. On Monday she still had fever but was more rational. She talked and laughed a great deal in a hoarse voice. On Tuesday her pulse was still slow and unequal; she slept a great deal and was very lightheaded. She asked for bread and ate it with good appetite. On Wednesday she was afebrile, and her pulse was "much amended." On Thursday she ate some chicken and attempted to walk but was too dizzy. In four or five days the "inequality" of her pulse stopped, and she was completely rational. She was amnesic about her execution and of events for two weeks prior to the event. The author says, ". . . when she came to herself again, she fell into the like speeches as she had used in prison before the execution: seeming there to go on where she had so long time left off." There remained for a month a ". . . giddiness in her head when she walked or stirred her body." After she was fully recovered, she repaired to the country, ". . . taking away with her the Coffin wherein she lay as a Trophey of this her wonder preservation."

Thus it is readily seen that severe strangulation can be followed by recovery after apparent death. Certain it is that this recovery may be only temporary and may be followed by relapse and death. There are at least two ways in which strangulation may be followed by recovery, or, as in the case of Desdemona, by partial recovery followed by coma and death. The first of these two mechanisms is that of laryngeal fracture as reported by Stevenson and Carling[12] in 1893 and by Thoinot[13] in 1904, but it is one which I do not think likely in the case of Desdemona. Whereas a patient may revive despite a fractured larynx, any words spoken would be croaking and unpleasant. Shakespeare would not desire his dying heroine to speak in harsh tones. However, temporary recovery followed by death due to laryngeal edema is a likely possibility.

I believe, however, that Desdemona probably died from multiple cerebral petechiae and cerebral degeneration caused by anoxia, these in turn due to pressure on the great blood vessels. She could have revived long enough to speak and again could have lapsed into coma and died. Gonzales, Vance and Helpern,[14] in their treatise on strangulation, stated that the color of the

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face of persons dying from strangulation is variable, sometimes being pale from pressure which constricts both the carotid arteries and jugular veins. Their conclusion was based on a large series of postmortem observations. The authors further stated that a person who is released one to three minutes after the strangulation has started, may live for a variable period, up to a few hours, and then succumb to the aftereffects on the brain and medullary centers. Such is the manner in which I believe Desdemona met an undeserved end.

SHAKESPEARE'S KNOWLEDGE OF RELEVANT SUBJECTS

Therefore, accepting the fact that Desdemona's manner of death as described by Shakespeare is compatible with physiologic concepts, it can be assumed, further, that the dramatist was writing realistically and was aware that death in such a sequence of events was possible. Garrison stated that the age of Shakespeare was pre-eminently a period of intense individualism, intellectual and spiritual, and that the great philosophers of the time were all concerned with aspects of natural science.

Medicine of the sixteenth and seventeenth centuries reached its highest attainment in England, and it was in London that Shakespeare was able to acquire the vast fund of medical knowledge he possessed. The greatest physician of the day was William Harvey, whose contributions to modern physiology need no elucidation here. It is germane to the subject of this paper, however, to note that although Harvey's treatise on the circulation was not published until twelve years after Shakespeare's death, references to the flow of blood are numerous in Shakespeare's plays. Warwick, in "The Second Part of King Henry the Sixth" (III, 2) spoke of the blood,

Being all descended to the laboring heart;
Who, in the conflict that holds with death,
Attracts the same for aidance 'gainst the enemy;
Which with the heart there cools and ne'er returneth
To blush and beautify the cheek again.

Dr. Witt suggested that Shakespeare may have been acquainted with Harvey. In any case, Shakespeare gives evidence of being as aware of an aspect of the physiology of circulation as the most eminent physicians of his time.

Othello appears to have been mentally deranged, at least for the time being, and the insight which Shakespeare possessed into mental ills has been the subject of many volumes. One need only mention the often-cited handwashing neurosis of Lady Macbeth to bring to mind the fountain of psychiatric knowledge present in these plays.

It is also pertinent to the present theme to realize that Shakespeare not only drew on his own astute observations to portray the mental derangements of Lear, or of Lady Macbeth, but also that he was familiar with the most recent medical literature pertaining to these matters. Theodore Spencer,[15] the eminent Shakespearean authority, has pointed out that in 1599, just before Shakespeare wrote "Hamlet," there appeared an English translation of a French medical work called, "Of the Diseases of Melancholy," by a certain Dr. Du Laurens, and that Du Laurens described a state of mind very similar to Hamlet's.

Miss Mary Isabele Sullivan,[16] in her treatise "Hamlet and Dr. Timothy Bright," has pointed out the parallels between Hamlet and the description of melancholy in Timothy Bright's "A Treatise of Melancholy" (1586). Spencer however, stated, "We cannot say that Shakespeare relied on any one text; he merely used the ideas which were part of the common knowledge of his time." This statement, by a Shakespearean scholar who was not trained in medicine, must be held as evidence that Shakespeare did possess the fundamentals of the medical knowledge of his time, and was familiar with medical literature. Certainly the plays contain many references to other aspects of medicine than strangling and mental illness, which are the subjects here.

More germane to the topic of Desdemona's death, however, is the opportunity Shakespeare had to observe public hangings, and thus make himself acquainted with the sequence of events in such an instance. The hanging cited previously, described in 1641, was not unlike the countless hangings exhibited to public view. Samuel Pepys, in his diary, fifty years after Shakespeare's death, described lucidly the public hangings that were still considered capital occasions for a day's outing. Certain it is that the members of Shakespeare's audience would be in a position to criticize a strangulation scene by virtue of their having themselves witnessed public hangings.

For the reasons above outlined; namely, the obvious familiarity of Shakespeare with the medical literature of his day and the opportunity he had to observe death by strangulation and to become acquainted with the manner of such a death, it must be concluded that Shakespeare was fully aware that the death of Desdemona, as he created it, was realistically and physiologically feasible.

TODAY'S ANSWERS TO FURNESS

In summary, I should like to offer the answers which I believe should be sent to Furness, were he to redistribute his questionnaire today:

1. It would be incompatible with the text for Othello to stab Desdemona.
2. If Othello had stabbed Desdemona, her smock could have been pale if hemorrhage had occurred only internally. This however is unlikely.
3. If she were strangled she could have been pale. This is borne out by reports of postmortem examination in cases of strangulation.
4. Desdemona could revive after apparent death, having been comatose due to cerebral anoxia.
5. Although she revived temporarily, Desdemona did not live because of injury to vital medullary centers by anoxia.
6. Desdemona really died from cerebral anoxia and permanent injury to vital centers in the brain stem.

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MAPHARSEN REACTION

QUESTION: A woman of 38 is being treated for lupus erythematosus. She gradually improved under gold (50 mg. IV weekly—top dose) therapy during a period of several months. Her lesions are plaque-like and are on her face and inside her mouth.

Therapy was changed to 0.02 gm. biweekly mapharsen in 5 cc. d.u. and after the third and fourth doses she experienced chills, fever (102° F.), and aching in her muscles. Mapharsen was tried because of reports in a 1947 issue of *Archives of Dermatology & Syphilology*.

Can you suggest possible reasons for the apparent reaction? A Wassermann test is to be done, but I do not feel that she is luetic.

M.D.—Windsor, Ontario

ANSWER: The reaction this patient is displaying to mapharsen indicates her intolerance to be arsenical, and is a warning sign of great importance. Further use of mapharsen should be discontinued immediately and not attempted again. Another explanation other than her intolerance to the arsenic is the possibility that the water or saline used for mixing the mapharsen was not chemically pure.

The reason for not continuing the injection of mapharsen is the possibility of the development of exfoliative dermatitis, hepatitis or neuritis, or all of them simultaneously. In addition, mapharsen is of but little value in the treatment of patients who have lupus erythematosus.

In two months or more it might be advisable to make a trial of bismuth subsalicylate, as used in the treatment of syphilis. The first few injections should be small, as for example, 0.5 cc. or less, in order to determine whether or not the patient also is intolerant to the bismuth. If she manifests no reaction, she could then be given 1 cc. of the bismuth subsalicylate every five days for a series of twelve or fourteen injections.

On the other hand, it would be possible to return again to the use of gold, since she seemed to derive some benefit from it previously. The patient should be instructed in regard to the avoidance of exposure to light.

CAUSE OF SEVERE BACKACHE

QUESTION: About eight or nine weeks ago this patient developed severe, sudden generalized backache. The pain was migratory and constant and did not appear to be relieved by rest. There was no history of injury or trauma. The pain seemed to pass to the "heart" and to the "abdomen" occasionally.

The laboratory tests were as follows: Kahn—negative; urinalysis—yellow, clear, acid; specific gravity 1.020; albumin and sugar negative; 3-4 WBC/hpf, a few epithelial cells; no blood in urine. The hemoglobin was 12.5 gm., RBC—4,380,000; WBC—9,800; neutrophiles—70; lymphocytes—26; eosinophiles—4.

X-ray examination was as follows: PA of the chest: heart and lungs were normal. There was fusiform central double density superimposed on the heart shadow to the left of the vertebral column. This posterior mediastinal mass seems to extend from the level of the sixth to the tenth dorsal vertebrae. There is complete destruction of the disc space between D-8 and D-9, irregular destruction without sclerosis of the approximating vertebral bodies of D-8 and D-9 with anterior wedging and early gibbus formation. There is equivocal destructive change in the pedicles of the lower dorsal vertebrae.

Diagnostic impression: Infectious spondylitis—etiology on an acid-fast basis involving the vertebral bodies of D-8 and D-9 with secondary kyphosis and paravertebral abscess formation.

X-ray of the chest at this time does not seem to show any active lesion and the patient was placed in a p. o. p. jacket from sacrum to upper dorsal region for immobilization.

The question now arises as to whether or not surgery is indicated in a case like this. The patient does not appear to be acutely ill and is bright and cheerful. Her general condition seems to be good. She is 26 years of age and a white female.

I should be very grateful for your opinion, recommended therapy and procedure in this case.

M.D.—Illinois

ANSWER: Judging from the history and report of the laboratory and x-ray examinations, the diagnosis of tuberculous spondylitis is quite feasible. The best procedure in her case, I believe, would be to have an orthopedic surgeon see her in consultation for consideration of fusion of the involved portion of the spine. Such an operation frequently hastens the healing process through the immobilization of the involved area of the spine.

TOAD PREGNANCY TEST

QUESTION: What are the advantages of the new pregnancy test in which toads are used? Is it reliable?

M.D.—Wisconsin

ANSWER: The pregnancy test by means of a male toad is similar to that of the somewhat better known use of the common frog (male) or the Rana pipiens. The principle is that the toad or the frog can be made to ejaculate spermatic fluid by its injection with a certain amount of urine from the patient being tested, if she is pregnant.

The experience in our Clinic with the male frog has been fairly satisfactory. The entire reliability of these tests has not yet been established, but they give promise of being fairly dependable.

PAUL TITUS

TOXIC GOITER

QUESTION: In toxic goiter treated with thiouracil compound, should the dosage be reduced after the symptoms have subsided? Can thiouracil be used with other medication for prolonged therapy?

M.D.—Missouri

ANSWER: Thiouracil should not be used in the treatment of hyperthyroidism because of its toxicity, but propyl thiouracil can be used along with iodine or any other medication for prolonged therapy of hyperthyroidism. If one is attempting to effect a definitive cure of the hyperthyroidism it is usually easier to maintain full dosage for a period of nine months to a year, supplemented with desiccated thyroid if symptoms of hypothyroidism develop, than it is to adjust the dose of propyl thiouracil. Following this the dosage can be gradually diminished and in many instances finally discontinued.

GEORGE CRILE, JR.

To The Editor:

In your January 1949 issue on page 79 there is a Question and Answer concerning brucellosis. I should like to point out that the modern therapy of this infection is indeed concerned with the use of newer antibiotics, the most successful as well as least toxic one being aureomycin. The previous use of streptomycin combined with sulfadiazine or sulfamerazine was reported by several investigators to be successful in a small number of cases particularly in the acute form. This combined therapy carries a definite risk of eighth nucleus damage, and in the chronic infection has not proved its worth. It is too early to state whether or not aureomycin is effective in the so-called chronic form which in the opinion of many careful investigators does actually exist.

The chief authorities for the use of these antibiotics are those which you quote but particularly W. W. Spink of Minneapolis and C. W. Eisele of Chicago, also Harris and others.

Mention, however, should be made of "vaccines" only to point out that the term is a misnomer since it was originally used to describe attenuated living cowpox and has since been corrupted to include bacterial suspensions, antigen solutions, and mixtures of broth extracts and bacterial derivatives. Under the latter classification comes the solution known as Brucellin as manufactured originally by Huddleson and later by a commercial drug house. These mixtures are not, as you imply, completely inert, but their efficiency in treatment is at least difficult to assess. I should like to call your attention to my own article in the Journal of the American Medical Association, Volume 130, pages 320-325.

Henry M. Benning, M.D.
7 East Mission Street
Santa Barbara, Calif.

TREATMENT OF AMEBIC DYSENTERY

QUESTION: What is your opinion of the use of emetine, bismuth and iodine in the treatment of amebic dysentery?

M.D.—Minnesota

ANSWER: Emetine bismuth iodide is an orally administered amebacide, highly recommended by some British authorities as an adjuvant to emetine therapy to prevent relapses and as the principal therapeutic agent in resistant chronic amebic dysentery. Its effectiveness is thought to be due to the direct action of released emetine on the bowel wall and contents, enhanced to some extent by the presence of the iodide. The drug has two serious drawbacks: it causes intense vomiting and diarrhea in most patients, and sufficient emetine may be absorbed to produce toxic effects if a full therapeutic dose is given.

Most American authorities have found carbarsone and diodoquin more effective and less toxic and, therefore, seldom employ emetine bismuth iodide. The drug has not been tried in our clinic.

FRANCIS G. BLAKE

PAGET'S DISEASE OF THE BREAST

QUESTION: Is there any beneficial treatment of Paget's disease of the breast of four years' duration?

M.D.—Illinois

ANSWER: Regardless of the duration of the lesion, once the diagnosis of Paget's disease of the breast is definitely established, radical amputation of the breast and removal of the axillary contents are indicated unless the deeper-lying duct carcinoma has advanced to a stage in which complete surgical removal of the tumor and all metastatic lesions cannot be accomplished.

The deeper duct carcinoma may not become manifest clinically for several years, and although much valuable time may be lost, it is usually of low-grade malignancy while still confined to the breast and is slow to metastasize to the axillary nodes. However, once metastatic involvement of the axilla occurs to any appreciable degree, the tumor acquires all the malignant characteristics of other mammary carcinomas, and the prognosis is poor.

R. LEE CLARK, JR.

ASCORBIC ACID

QUESTION: Is sodium ascorbate or ascorbic acid of any value in refractory cases of allergy?

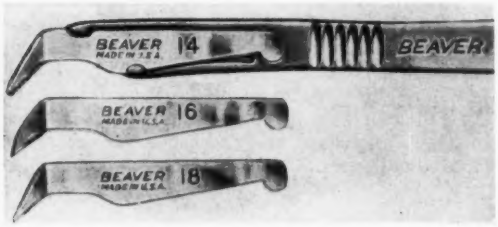
M.D.—New York

ANSWER: Sodium ascorbate and ascorbic acid have been used and their effects thoroughly studied by many excellent investigators. The consensus is that these preparations are of no value in the treatment of any allergic diseases.

HARRY L. ROGERS

New Drugs and Instruments

Information published in this department has been supplied by the manufacturers of the products described.



BENT BLADES FOR THE BEAVER KNIFE

DESCRIPTION: These blades fit all Beaver knife handles; the handles are 5 and 7 inches long. Available in three styles: No. 14, sharp all 'round; No. 16, sharp on one edge only; and No. 18, sharp on both edges, but with dull, safe point.
PRODUCER: Rudolph Beaver, Waltham 54, Mass.

CHLOROMYCETIN

PURPOSE: Antibiotic.
DESCRIPTION: Chloromycetin (chloramphenicol) is a crystalline substance obtained from cultures of *Streptomyces venezuelae* or prepared synthetically.
INDICATIONS FOR USE: Enteric infections, notably typhoid fever and other salmonella infections, bacillary urinary infections, and diseases in which the rickettsias are etiologic factors are among the conditions which yield to Chloromycetin therapy. Effectiveness is indicated in atypical pneumonia, psittacosis, undulant fever, Rocky Mountain spotted fever, typhus, scrub typhus, and lymphogranuloma venereum.
DOSAGE AND ADMINISTRATION: Length of treatment is variable and dependent on the character of the infection. Present dosage regimens are based on clinical experience gained thus far and may be modified in light of future experience.

Use of smaller doses increases possibility of relapse. Optimal dosage given at intervals around the clock is necessary to assure maximum effectiveness.

HOW SUPPLIED: In Kapseals, each containing 0.25 gm., in packages of 12.
PRODUCER: Parke, Davis & Company, Detroit 32, Mich.

PENALEV TABLETS

PURPOSE: Tablet form of penicillin for use in inhalation therapy, sublingual administration, oral use in pediatrics, and in prescription compounding.
DESCRIPTION: Penalev Tablets provide 50,000 units of penicillin, are readily dissolved in water, salt solution, milk formulas, and saliva. They retain potency at room temperature for thirty-six months.
HOW SUPPLIED: In rubber-stoppered vials with aluminum seal caps, 12 tablets in a vial.
PRODUCER: Sharp & Dohme, Inc., Philadelphia, Pa.

ALTERNATING PRESSURE MATTRESS

PURPOSE: Aid in prevention and treatment of bedsores.
DESCRIPTION: Constructed of Velon, a Firestone plastic film, the mattress consists of a series of air cells 1¼ inches in diameter running its width transversely. Alternate cells are connected to a manifold which forms the edge of the mattress. The two systems of interspersed cells are alternately deflated and inflated at short intervals by a small electrically driven pump.
PRODUCER: Firestone Plastics Company and the H. J. Rand Foundation, Cleveland, Ohio.

DRAMAMINE

PURPOSE: Prevention and control of motion sickness.
COMPOSITION: β-dimethylaminoethyl benzohydryl ether 8-chlorotheophyllinate.
DOSAGE AND ADMINISTRATION: Recommended dosage is 50 to 100 mg. 4 times daily depending on severity of motion.
HOW SUPPLIED: In 100 mg. scored tablets.
PRODUCER: G. D. Searle & Co., Chicago, Ill.

DECUPRYL

PURPOSE: Skin fungicide.
COMPOSITION: A solution of copper undecylenate 10 per cent, undecylenic acid 5 per cent, dioctyl sodium sulfosuccinate 0.2 per cent in a fat-solvent liquid containing equal parts of tetrachloroethylene and isopropanol.
INDICATIONS FOR USE: In Tinea capitis, dermatophytosis, Tinea cruris, and other fungus infections of the skin.
DOSAGE AND ADMINISTRATION: The affected areas are painted with the solution after cleansing and drying thoroughly, once or twice a day.
CAUTION: Any severe inflammation in cases of dermatophytosis should be reduced before treatment is begun with Decupryl.
HOW SUPPLIED: 1-ounce bottle with applicator brush and 4-ounce bulk bottle.
PRODUCER: Crookes Laboratories, New York 17, N.Y.

LUMETRON HEMOGLOBIN AND GLUCOSE METER MODEL 15

PURPOSE: Photoelectric instrument for determination of hemoglobin and glucose.

DESCRIPTION: The instrument is furnished in a wooden housing with cover and carrying strap. A blood pipette for hemoglobin and 2 glass cells are fastened inside the instrument cover. Operates on the AC power line. Glucose in blood can be determined either according to a macro procedure with 1 ml. blood from venipuncture or according to a micro procedure with 0.1 ml. blood from the fingertip. The micro test is carried out with the same reagents and technic as the macro test. The urine glucose determination is based on a method which requires dilution with sodium carbonate solution and subsequent boiling.

PRODUCER: Photovolt Corporation, New York, N.Y.

INOSITOL

PURPOSE: Treatment of diseases associated with abnormal fat and lipid deposition.

DESCRIPTION: Clinical experience to date indicates that Inositol is capable of preventing fat deposition in the livers of patients kept on diets which are known to produce fatty infiltration. In addition, it appears capable of reducing blood cholesterol and cholesterol ester levels in hypercholesterolemia.

HOW SUPPLIED: In 0.5 gm. capsules.

PRODUCER: C.S.C. Pharmaceuticals, division of Commercial Solvents Corporation, Terre Haute, Ind.

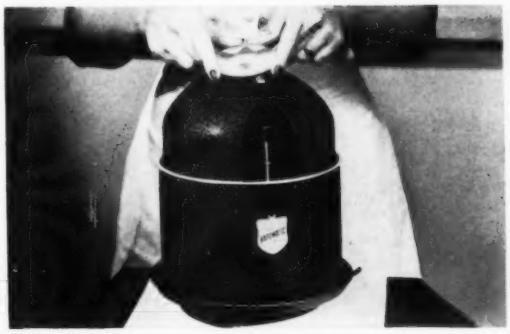
TERSAVIN

PURPOSE: Treatment of sinus infections.

COMPOSITION: Crystalline l-ephedrine salt of penicillin G.

HOW SUPPLIED: In packages of 8 foil-wrapped tablets, containing 30 mg. of Tersavin (equivalent to 30,000 units of penicillin G and 9.9 mg. of l-ephedrine), with a bottle graduated at 7.5 cc. in which the solution may be made.

PRODUCER: Hoffmann-La Roche, Inc., Nutley, N.J.



VAPOMATIC VAPORIZER

DESCRIPTION: Generates an antiseptic invisible cloud of glycol that disinfects the air. The Vapomatic operates from any standard light outlet.

PRODUCER: Merit Western Products Co., Alhambra, Calif.

BACIDRIN*

PURPOSE: Treatment of upper respiratory infections associated with inflammation and congestion of the nasal mucosa.

COMPOSITION: The dry contents of one bottle dissolved in a sufficient quantity of water to fill the bottle makes 15 cc. of solution containing:

Bacitracin	200 units
Ephedrine hydrochloride	5 mg. (0.5 per cent)
Myristyl-gamma-picolinium chloride	1:10,000

DOSAGE AND ADMINISTRATION: The solution may be administered every two to four hours as a nose drop or by nasal atomizer.

CAUTION: After the solution has been prepared, it should be stored in a refrigerator and used within one week. In the dry state, it is stable for one year.

HOW SUPPLIED: 15 cc. bottle with dropper.

PRODUCER: The Upjohn Company, Kalamazoo, Mich.

*Trade Mark.

MONITAN

DESCRIPTION: Liquid solution of sorbitan mono-oleate polyoxyethylene derivative for use in abnormal physiologic conditions with impaired absorption of fats or fat soluble substances from the small intestines.

COMPOSITION: Each teaspoonful of Monitan contains 1.5 gm. of S.M.P.D.

INDICATIONS FOR USE: In malnutrition due to faulty fat absorption, intestinal hyper- or hypoactivity, regional enteritis, pancreatic fibrosis, sprue, celiac disease, impaired biliary cycle; fecal fat in excess of 4 per cent.

DOSAGE AND ADMINISTRATION: Adults—1 to 2 teaspoonsful three times daily with meals, or as prescribed by the physician. Children—¼ teaspoonful with meals, as required.

CAUTION: Mineral oil and mineral oil emulsions are contraindicated during administration of Monitan.

HOW SUPPLIED: In 12-ounce bottles.

PRODUCER: Ives-Cameron Company, Inc., New York, N.Y.

MODEL 2050 ION CHAMBER CHARGER-READER

PURPOSE: For use in conjunction with pocket type ionization chambers; the latter are used as health monitoring devices in the presence of gamma or x-ray types of radiation.

DESCRIPTION: The functions of Model 2050: (1) charge ion chamber to a known voltage, and (2) measure residual chamber charge after exposure to radiation. This 110 volt AC operated electronic voltmeter and electrometer will charge and read the NUCLEAR Model 3340 diaphragm type pocket meter, and by rotation of a selector switch, the nondiaphragm type pocket ion chamber can also be checked. All "charge" and "read" observations are made on a 3-inch meter with a linear scaler. The cabinet measures 6 by 5 by 10½ inches, and provision is made for storing up to seven pocket ion chambers within the case cover.

PRODUCER: Nuclear Instrument & Chemical Corporation, Chicago 10, Ill.

PROCAINE PENICILLIN G

DESCRIPTION: When uniformly suspended with a specified amount of diluent, sterile distilled water, normal saline, or dextrose, each 1 cc. will contain 300,000 units of Procaine Penicillin in chemical combination with approximately 120 mg. of Procaine base.

HOW SUPPLIED: In 5 dose vials, each containing 1,500,000 units.

PRODUCER: Winthrop-Stearns, Inc., New York, N.Y.

MERCY COMBINATION BASSINET-DRESSING TABLE

PURPOSE: Protection of the newborn infant against airborne bacteria and cross-infection.

DESCRIPTION: In either enameled or stainless steel, this combination bassinet and dressing table has safety glass shields on three sides; one shield lowers to provide access to the infant. The cabinet unit slides forward and its top serves as a dressing table. A quarter-circle drawer swings out to hold necessary utensils. There is also a storage compartment, with a disappearing-type door, for sterile linen and other supplies.

PRODUCER: S. Blickman, Inc., New York, N.Y.

WHITE PETROLATUM U.S.P.—STERILE

PURPOSE: For topical application, direct from collapsible tubes, to burns and wounds, in packs, drains, protective coverings, or as a lubricant for gloves, catheters, and instruments.

DESCRIPTION: Retains all the properties of white petrolatum, namely, unchanged color, freedom from odor, and the same consistency, viscosity, and melting point, after sterilization.

HOW SUPPLIED: In 1-ounce collapsible tubes, packed 6 to a carton.

PRODUCER: Baybank Pharmaceuticals, Inc., New York, N.Y.

Leaves from a Doctor's Diary

By Maurice Chideckel

May 1 . . . I hacked my way over violently hostile terrain in that subterranean den, Tony's rooming place, peopled with wrecks that once were men. Fate cast them adrift, exercised its disturbing evils, shattered and crushed them. As I was passing through the long, dark, and ill-smelling basement, they cursed and threatened, and demanded money for drinks.

From the far corner came agonizing moans. I followed the heartbreaking sounds and located my patient, whose bloodless face looked terrifying by the flickering oil lamp. Great Heavens! Richard Bedford, or a distorted image of him. Shudderingly I gazed at this once cultured man, who had the crowning grace of courage. Something went wrong with him suddenly. He lost the ability to keep any fixed course. His contradictory efforts not only hampered his progress in any undertaking, bringing about a rapid descent, but it made his life an existence of intermittent torment. Then he let go. Happiness eluded him. The woman he loved betrayed him; others rebuffed or palled on him. He sank low and one woman he forced into a life of shame.

Here he was, a degraded creature, dying of a huge dose of oxalic acid. The container was on the table. Near it was a letter addressed to his mother in New York, and there was also a note for me. He begged me to make no effort to save him. "The streetwalker I picked up today was Grace, beautiful Grace, for whose moral crimes I am responsible." As I was about to tear out plaster from the wall to get some form of lime, Richard Bedford expired. I hastened outside. The foul air in the basement was suffocating.

Near that miserable boarding house I was met by a young man who informed me that he was a second year medical student, and that he had rendered first aid—pumped his stomach and administered potassium salt—the very things he should not have done, and the very drug he should not have given. His treatment undoubtedly hastened Bedford's death. And these men have been told time and again, that if you don't know what to do, do nothing.

I took the letter to mail it at the railroad station. An elderly, well dressed woman arrested my attention by her running from one ticket office window to the other, about eight in number. She spoke angrily to each ticket seller, and finally, with disgust, ran over to a man. "No use," she spoke resignedly, "those highway robbers must have a union. They all demand the same price for a ticket to New York."

* * *

May 2 . . . Two middle-aged women, sisters, discussed their daughters in my waiting room. "My Hilda, tomorrow she will be thirty, and no prospect. Oh, her advancing years. They are killing me."

The other woman cried as she talked. "My Leona. Lord help me. Her advancing months drive me to to the grave. I'll kill myself. Sure, anybody can notice it. No, she does not remember how and who. And you are complaining yet."

* * *

May 3 . . . Somehow the advanced case of laryngeal carcinoma and the case of rickettsialpox traced to mice in the apartment incinerator had a depressing effect on the usually cheerful Dr. Jay Floyd. He became gloomily philosophical. "I am viewing the future with forebodings. Wherever I look I see symptoms of decadence. I just read Auguste Comte, the man who coined the word sociology and who expressed the aspirations and cherished ambitions of his time and community. What are present-day humanity's cherished ambitions? None. Every one wants to dominate. Future generations——."

"Will not have laryngeal malignancies," I interrupted, as he was about to plunge into an endless diatribe. "There will be no mice to transmit and disseminate disease. Evil and corruption may be a part of civilization. So are progress and good will. And why worry about a future when your bones and mine will have long crumbled into dust?"

Floyd's good humor returned when Father Alva approached us and remonstrated with him why he no longer comes to church on Sunday. "Have you become a Seventh-Day Adventist?" the clergyman asked him. "No, Father, my work forced me to become a Seventh-Day Absentist."

Said Dr. Scott: "It's well to remember that peripheral neuritis is quite often the cause of acute deficiency of vitamin B_1." "And it's well to remember," broke in his daughter, "that I need a few new dresses, shoes, pocketbooks, and hats. What I have now belongs to another generation. Cough up five hundred dollars, Pop. Come on." "Five hundred dollars," he repeated, as he sat down to write a check. "She finished high school, and she finished college. And now she is finishing me."

* * *

May 9 . . . So many lives have been shaped and molded and ruined by gossiping women who find delight in the assassination of characters and in the wrecking of one's

future. Betty Hume had a short-lived romance. A young man called on her several times and then vanished. Betty's abdomen became large suddenly, due to a huge fibroma that was rapidly developing in her uterus. The neighboring woman noticed it, winked, whispered, then talked aloud.

Betty went to New York where lived her only sister and there she underwent a hysterectomy. The sister, afflicted with a cardiac condition, died in labor. The baby was delivered alive by the cesarean route. Betty adopted the little girl and brought it back with her. A clear cut case of a birth without the benefit of clergy.

I stood among the group, all church members, and clarified or tried to clarify this unusual episode. But they nodded their heads significantly. Her life in the neighborhood became intolerable. She was constantly threatened with violence. On the suggestion of my wife she was taken into my house for protection, until some way can be found to make her life secure.

Said a rough voice through the phone. "Now, you see. You are the kid's father. Some fine gentleman." I am avoiding the neighborhood. Anyhow, my election to fatherhood was unanimous. Today Betty received a letter from a lawyer, asking if she wished to institute suit against me for the permanent maintenance of the girl and herself.

* * *

May 12 . . . The life of colleague Kenneth was crowned and crowded with many achievements. I always admired his humorous acceptance of life. Whenever I looked at him I experienced a sense of timelessness. At an advanced age, he looks vigorously youthful. He once told me that he thinks he is the only man to whom nothing happened. Now it did. He is being sued for fifty thousand dollars for causing the death of Marks Palmer.

It was a seropositive case of cardiovascular syphilis; 850,000 units of penicillin were administered by Dr. Kenneth. Soon the patient developed Jarisch-Herxheimer reaction—chills, fever, malaise, edema, cellular infiltration and, suddenly, death.

Thundered the legal light: "Do you know the oath of Hippocrates that was taken by members of the school at Cos?" His honor came to life and wanted to know in what state Cos was. The lawyer continued. "In that oath you swore that, I will give no deadly medicine to anyone; why, I am asking you, why did you give it to Marks Palmer?" Confused, the doctor looked at the judge, at the jury, at me, at his wife, and said nothing. He only smiled sheepishly.

The lawyer for the defense put me on the stand to testify in behalf of my colleague. I told the judge and jury that since Hippocrates was mentioned, I will state that the description by Charles Singer of that ancient healer fits perfectly the defendant. "In beauty and dignity that figure is beyond praise. He will ever remain the type of the perfect physician. Learned, observant, humane with a profound reverence for the claims of his patients, pure of mind and master of his passions."

I then informed the court that Dr. Kenneth, for ethical reasons, could not reveal the nature of the illness of his patient. Marks Palmer was not my patient. Here is his hospital record. Syphilis invaded his heart and blood vessels. This alone kills. Dr. Kenneth wanted to give his patient the benefit of any possible hope to save and prolong his life. Penicillin usually fails in such cases. It seldom cures. The deceased was not killed by penicillin, but by syphilis; the germ simply refused to be destroyed by any antibiotic.

While the jury was deliberating, Dr. Kenneth asked his lawyer whether in case the suit for fifty thousand dollars is decided against him, would they accept the payment of one dollar a week. It's the best he could do. The doctor won. Going out of the courtroom he wanted to know if he was really as good as I described him, or was I lying deliberately?

* * *

May 16 . . . Two or three years ago I read a book about Charleston, the city of sorcery and mystery, wherein an eccentric physician fell in love with the wraith of a beautiful woman.

The wraith of another woman, now dead almost a century, disintegrated the domestic life of Dr. Fechner and his wife, whose temperaments were never attuned to one another. Now came the climax. Fechner happened to read the life of Dorothea Lynde Dix, the great American woman. It is to her that we owe the erection of modern mental hospitals, the abolition of brutality and the humane treatment of the inmates. In his sleep he repeatedly mentioned Dorothea Lynde Dix, and once when his wife shook him to ask who she was he merely answered, "A wonderful woman."

Last week she left him. She refused to return until she sees that female, face to face. Yesterday she instituted suit for divorce, naming Dorothea Lynde Dix as correspondent. The doctor made no effort to prove his innocence, nor to contest the divorce. "I'll tell you," he finally confided in me, "I told no one about my marital disillusionment. I always wanted a divorce, hoping to marry someone of estimable qualities. I had no ground. Now the dead came to my rescue. I wrote to that corpse, left the letters on my desk. Her lawyer has got

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them now. Believe it or not, my practice increased considerably. Old maids, widows, divorced women, and others looking for a mate are flocking to my office. Dorothea Lynde Dix, I worship you."

* * *

May 25 . . . Passing events. A crowded house with excitable people because of an asthmatic attack in a middle-aged woman. Administration of epinephrine by colleague Russell. Face became swollen at once, and eyes closed. Dr. Russell jumped through the window on the ground floor to escape lynching.

Same house, next day. Second degree burn. Application of butesin picrate by me. Violent eczematous dermatitis. Second floor. Fists clenched. Voices loud and angry. "Kill him," cried one inebriated American. "No killin,' just let him have it in the peepers." Another infuriated voice: "Peepers, nothing. In the kisser, break his smeller."

Situation desperate. They seemed to settle for the smeller. I gazed about. Outside Officer McGann, whom I know well was leaning leisurely against a lamp post. A large glass pitcher was on the table. I threw it at the window. The broken panes and the pitcher that broke on the sidewalk attracted the policeman's attention. He came up running and he opened the door the moment I was to be struck. I ducked, the fist landed on his "smeller" as I hurriedly ran out and down.

I was telling Mary, my wife, of the dashing things I have done. I felt myself shrinking as she looked down on me. "Running out. Courageous. Have the policeman's nose take the rap for yours. Dashing things. Hmm."

Anxiety, impaired memory eventuating into complete amnesia, delusions and hallucinations. I took a blood test. There was a marked case of hypoglycemia. Patient, a young woman, restored to complete normalcy. And I am a professor, the greatest on the globe.

Thyrotoxicosis with exophthalmos. Operation on my advice. Ocular protrusion worse. Progression of proptosis threatens loss of vision. And I am a bum, a shoemaker and one to be avoided.

Such is the practice of medicine. Like life itself events tormenting or enticing, soaring and descending, the spirit enlightened, distracted and impeded. Praised, cursed, hated, and adored, opinions coagulate into speculations, and the opinions sink and swim with tide and time; they speak in banalities and in high praise, conjectures are turned into certainties, hastily gathered impressions.

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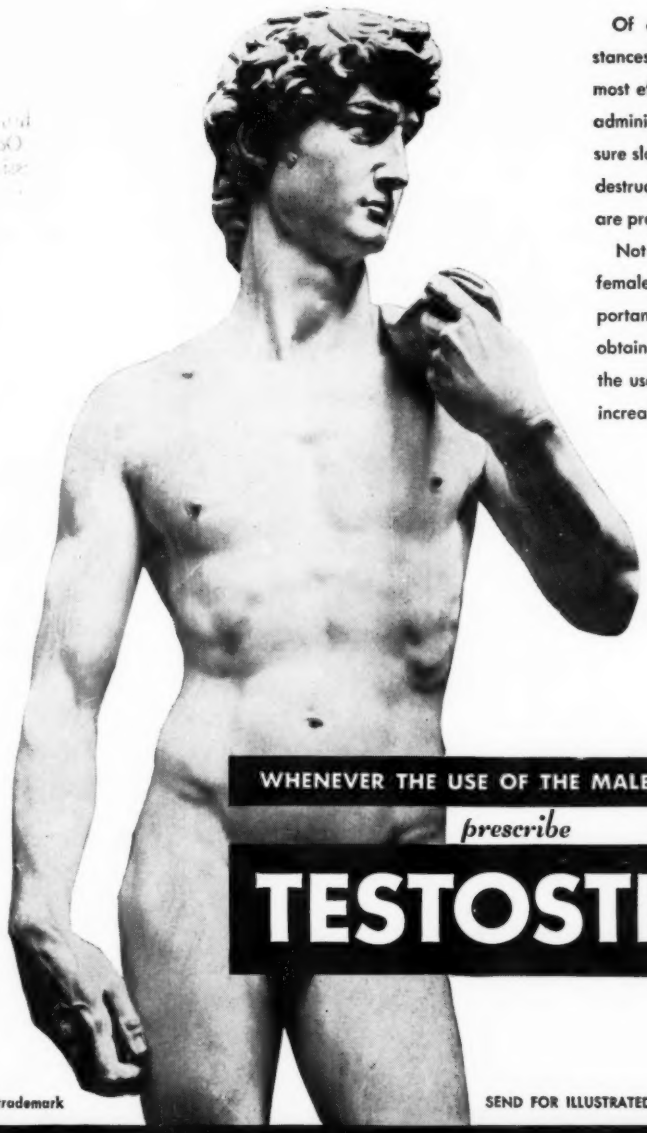

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1. Friedlaender, A. S., and Friedlaender, S.: Annals of Allergy, 6: 23-29, Jan.-Feb., 1948.

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